10/660,118

```
=> d his nofile

     (FILE 'HOME' ENTERED AT 14:47:35 ON 23 FEB 2006)

     FILE 'CAPLUS' ENTERED AT 14:47:57 ON 23 FEB 2006
                SET LINE 250
                SET DETAIL OFF
                E US2003-660118/AP,PRN 25
                SET NOTICE 1000 SEARCH
L1            1 SEA ABB=ON  US2003-660118/AP
                SET NOTICE LOGIN SEARCH
                SET LINE LOGIN
                SET DETAIL LOGIN
                D SCAN
                SEL RN

     FILE 'REGISTRY' ENTERED AT 14:50:02 ON 23 FEB 2006
L2           21 SEA ABB=ON  (117525-18-5/BI OR 117525-19-6/BI OR 3483-12-3/BI
                OR 53-57-6/BI OR 616-91-1/BI OR 675214-32-1/BI OR 675214-33-2/B
                I OR 675214-34-3/BI OR 675214-35-4/BI OR 675214-36-5/BI OR
                675214-37-6/BI OR 675214-38-7/BI OR 675214-39-8/BI OR 675214-40
                -1/BI OR 675214-41-2/BI OR 675214-42-3/BI OR 675214-43-4/BI OR
                675625-84-0/BI OR 675625-85-1/BI OR 70-18-8/BI OR 9074-14-0/BI)

                D SCAN

     FILE 'CAPLUS' ENTERED AT 14:53:26 ON 23 FEB 2006
L3         2951 SEA ABB=ON  WHITE C?/AU
L4         4538 SEA ABB=ON  THIOREDOXIN#/OBI
L5            9 SEA ABB=ON  L3 AND L4
L6         2350 SEA ABB=ON  SPUTUM/CT
L7         4370 SEA ABB=ON  MUCUS/CT
L8         9174 SEA ABB=ON  CYSTIC FIBROSIS/OBI
L9           27 SEA ABB=ON  L4 AND (L6 OR L7 OR L8)
L10           9 SEA ABB=ON  L4 AND (L6 OR L7)
                D SCAN
L11        3325 SEA ABB=ON  THIOREDOXINS/CT
L12           7 SEA ABB=ON  L11 AND (L6 OR L7)
L13      728128 SEA ABB=ON  9/SC,SX
L14           4 SEA ABB=ON  L12 NOT L13
L15           3 SEA ABB=ON  L12 AND L13
                D SCAN
L16         472 SEA ABB=ON  MUCOLY?/OBI
L17       29200 SEA ABB=ON  LIQUEF?/OBI
                E LIQUIDIFI/CT
                E LIQUIDIFI/BI
L18      161373 SEA ABB=ON  VISCO?/OBI
L19        1055 SEA ABB=ON  EXPECTORANT#/OBI
L20          12 SEA ABB=ON  L11 AND L8 NOT L13
L21           8 SEA ABB=ON  L20 NOT (L1 OR L5 OR L14)
                D SCAN
L22        7029 SEA ABB=ON  CYSTIC FIBROSIS/CT
L23           5 SEA ABB=ON  L22 AND L11 NOT (L13 OR L1 OR L5 OR L14)
                D SCAN TI

     FILE 'REGISTRY' ENTERED AT 15:19:04 ON 23 FEB 2006
L24      541003 SEA ABB=ON  .C..C./SQSP

     FILE 'CAPLUS' ENTERED AT 15:19:39 ON 23 FEB 2006
```

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     FILE 'REGISTRY' ENTERED AT 15:19:48 ON 23 FEB 2006
                D RN L24 270000
L25         271004 SEA RAN=(,518362-12-4) ABB=ON  .C..C./SQSP
L26         269999 SEA ABB=ON  L24 NOT L25

     FILE 'CAPLUS' ENTERED AT 15:21:37 ON 23 FEB 2006
L27          58456 SEA ABB=ON  L25 OR L26
L28            389 SEA ABB=ON  L27 AND L11
L29             82 SEA ABB=ON  L27 AND (L6 OR L7)
L30              8 SEA ABB=ON  L29 AND (L16 OR L17 OR L18 OR L19)
                   D SCAN TI

     FILE 'REGISTRY' ENTERED AT 15:25:54 ON 23 FEB 2006
L31           5728 SEA ABB=ON  CGPC/SQSP

     FILE 'CAPLUS' ENTERED AT 15:26:20 ON 23 FEB 2006
L32           2177 SEA ABB=ON  L31
L33              8 SEA ABB=ON  L32 AND (L6 OR L7)
L34              2 SEA ABB=ON  L30 AND L33
                   D SCAN TI L33

     FILE 'MEDLINE' ENTERED AT 15:27:56 ON 23 FEB 2006
                E THIOREDOXIN/CT
                E E3+ALL
L35           2163 SEA ABB=ON  THIOREDOXIN/CT
L36           2181 SEA ABB=ON  WHITE C?/AU
L37              7 SEA ABB=ON  L35 AND L36
                   D TRIAL 1-7
L38          11646 SEA ABB=ON  SPUTUM/CT
L39          13832 SEA ABB=ON  VISCOSITY/CT
                E MUCUS+ALL/CT
L40           8697 SEA ABB=ON  MUCUS+NT/CT
L41              1 SEA ABB=ON  L35 AND L39 AND (L38 OR L40)
L42              3 SEA ABB=ON  L35 AND (L38 OR L39 OR L40)
                   D TRIAL 1-3
L43          19620 SEA ABB=ON  CYSTIC FIBROSIS/CT
L44              2 SEA ABB=ON  L43 AND L35

     FILE 'EMBASE' ENTERED AT 15:31:48 ON 23 FEB 2006
L45           1505 SEA ABB=ON  WHITE C?/AU
                E THIOREDOXIN+ALL/CT
L46           2331 SEA ABB=ON  THIOREDOXIN/CT
                E MUCUS+ALL/CT
L47           6283 SEA ABB=ON  MUCUS+NT/CT
                E SPUTUM+ALL/CT
L48           3562 SEA ABB=ON  SPUTUM/CT
                E VISCOSITY+ALL/CT
L49            100 SEA ABB=ON  SPUTUM VISCOSITY/CT
L50           3436 SEA ABB=ON  VISCOELASTICITY/CT
L51           9749 SEA ABB=ON  VISCOSITY/CT
L*** DEL         8 S L45 AND L46
                   D TRIAL 1-8
L52            267 SEA ABB=ON  MUCOLYSIS/CT
L53            183 SEA ABB=ON  LIQUEFACTION/CT
L54              8 SEA ABB=ON  L45 AND L46
L55              5 SEA ABB=ON  L46 AND (L47 OR L48 OR L49 OR L50 OR L51 OR L52 OR
                   L53)
                E CYSTIC FIBROSIS+ALL/CT
L56          20389 SEA ABB=ON  CYSTIC FIBROSIS/CT
L57              7 SEA ABB=ON  L46 AND L56
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L58           4 SEA ABB=ON  L57 NOT (L54 OR L55)
                D TRIAL 1-4
L59           1 SEA ABB=ON  L46(L)DT/CT AND L56

     FILE 'DRUGU' ENTERED AT 15:36:48 ON 23 FEB 2006
L60         356 SEA ABB=ON  WHITE C?/AU
                E THIOREDOXIN/CT
L61          72 SEA ABB=ON  THIOREDOXIN#/CT
L62           2 SEA ABB=ON  L60 AND L61
                D TRIAL 1-2
L63         405 SEA ABB=ON  CYSTIC-FIBROSIS/CT
L64        1059 SEA ABB=ON  SPUTUM/CT
L65        4493 SEA ABB=ON  MUCOLYTIC#/CT
                E MUCUS/CT
L66         972 SEA ABB=ON  MUCUS/CT
                E VISCOSITY/CT
                E E3+ALL
L67        2111 SEA ABB=ON  VISCOSITY/CT
                E LIQUEF/CT
L68          14 SEA ABB=ON  LIQUEFACTION/CT OR LIQUEFYING/CT
L69           3 SEA ABB=ON  L61 AND (L63 OR L64 OR L65 OR L66 OR L67 OR L68)
                D TRIAL 1-3
L70       45091 SEA ABB=ON  RESPIRATORY/CC
L71           1 SEA ABB=ON  L61 AND (L63 OR L64 OR L65 OR L66 OR L67 OR L68)
                AND L70

     FILE 'STNGUIDE' ENTERED AT 15:40:45 ON 23 FEB 2006

     FILE 'JICST-EPLUS, PASCAL, WPIX, IPA, BIOSIS, ESBIOBASE, BIOTECHDS,
     LIFESCI, CONFSCI, DISSABS, SCISEARCH' ENTERED AT 15:47:40 ON 23 FEB 2006
L72       11489 SEA ABB=ON  WHITE C?/AU
L73       17233 SEA ABB=ON  THIOREDOXIN#
L74       38537 SEA ABB=ON  SPUTUM
L75       47183 SEA ABB=ON  MUCUS
L76        3898 SEA ABB=ON  MUCOLY?
L77       74427 SEA ABB=ON  LIQUEF?
L78      567528 SEA ABB=ON  VISCO?
L79       79051 SEA ABB=ON  CYSTIC FIBROSIS
L80          10 SEA ABB=ON  L72 AND L73 AND (L74 OR L75 OR L76 OR L77 OR L78
                OR L79)
L81           8 SEA ABB=ON  L73 AND L76
L82          14 SEA ABB=ON  L73 AND (L74 OR L75) AND (L77 OR L78 OR L79)

     FILE 'STNGUIDE' ENTERED AT 15:50:22 ON 23 FEB 2006

     FILE 'CAPLUS' ENTERED AT 15:51:08 ON 23 FEB 2006
                D QUE L1
                D QUE L5
L83           9 SEA ABB=ON  L1 OR L5

     FILE 'MEDLINE' ENTERED AT 15:51:08 ON 23 FEB 2006
                D QUE L37

     FILE 'EMBASE' ENTERED AT 15:51:08 ON 23 FEB 2006
                D QUE L54

     FILE 'DRUGU' ENTERED AT 15:51:08 ON 23 FEB 2006
                D QUE L62

     FILE 'JICST-EPLUS, PASCAL, WPIX, IPA, BIOSIS, ESBIOBASE, BIOTECHDS,
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     LIFESCI, CONFSCI, DISSABS, SCISEARCH' ENTERED AT 15:51:25 ON 23 FEB 2006
                D QUE L80

     FILE 'MEDLINE, DRUGU, CAPLUS, EMBASE, PASCAL, WPIX, BIOSIS, ESBIOBASE,
     BIOTECHDS, SCISEARCH' ENTERED AT 15:51:39 ON 23 FEB 2006
L84           20 DUP REM L37 L62 L83 L54 L80 (16 DUPLICATES REMOVED)
                     ANSWERS '1-7' FROM FILE MEDLINE
                     ANSWERS '8-9' FROM FILE DRUGU
                     ANSWERS '10-13' FROM FILE CAPLUS
                     ANSWERS '14-16' FROM FILE EMBASE
                     ANSWERS '17-18' FROM FILE PASCAL
                     ANSWERS '19-20' FROM FILE ESBIOBASE
                D IALL 1-9
                D IBIB ED ABS HITIND 10-13
                D IALL 14-20

     FILE 'MEDLINE' ENTERED AT 15:52:20 ON 23 FEB 2006

     FILE 'STNGUIDE' ENTERED AT 15:52:47 ON 23 FEB 2006

     FILE 'REGISTRY' ENTERED AT 15:53:28 ON 23 FEB 2006
                D QUE L24

     FILE 'CAPLUS' ENTERED AT 15:53:28 ON 23 FEB 2006
                D QUE L30
L85            6 SEA ABB=ON  L30 NOT L83
                D IBIB ED ABS HITRN L85 1-6
                SEL HIT RN L85 1-6

     FILE 'STNGUIDE' ENTERED AT 15:54:51 ON 23 FEB 2006

     FILE 'REGISTRY' ENTERED AT 15:55:07 ON 23 FEB 2006
L86           98 SEA ABB=ON  (132053-08-8/BI OR 143831-71-4/BI OR 132053-07-7/BI
                  OR 182177-07-7/BI OR 182177-08-8/BI OR 182177-09-9/BI OR
                 182177-10-2/BI OR 182177-11-3/BI OR 182177-12-4/BI OR 182177-13
                 -5/BI OR 182177-14-6/BI OR 182177-15-7/BI OR 182177-16-8/BI OR
                 182177-17-9/BI OR 182177-18-0/BI OR 182177-19-1/BI OR 182177-20
                 -4/BI OR 182177-21-5/BI OR 182177-22-6/BI OR 182177-23-7/BI OR
                 182177-24-8/BI OR 182177-25-9/BI OR 182177-26-0/BI OR 182177-27
                 -1/BI OR 182177-28-2/BI OR 182177-29-3/BI OR 182177-30-6/BI OR
                 182177-31-7/BI OR 182177-32-8/BI OR 182177-33-9/BI OR 182177-34
                 -0/BI OR 182177-35-1/BI OR 182177-36-2/BI OR 182177-37-3/BI OR
                 182177-38-4/BI OR 182177-39-5/BI OR 182177-40-8/BI OR 182177-41
                 -9/BI OR 182177-42-0/BI OR 182177-43-1/BI OR 182177-44-2/BI OR
                 182177-45-3/BI OR 182177-46-4/BI OR 182177-47-5/BI OR 182177-48
                 -6/BI OR 182177-49-7/BI OR 182177-50-0/BI OR 182177-51-1/BI OR
                 182177-52-2/BI OR 182177-53-3/BI OR 182177-54-4/BI OR 182177-55
                 -5/BI OR 182177-56-6/BI OR 182177-57-7/BI OR 182177-58-8/BI OR
                 182177-59-9/BI OR 182177-60-2/BI OR 182177-61-3/BI OR 182177-62
                 -4/BI OR 182177-63-5/BI OR 182177-64-6/BI OR 182177-65-7/BI OR
                 182177-66-8/BI OR 182177-67-9/BI OR 182177-68-0/BI OR 182177-69
                 -1/BI OR 182177-70-4/BI OR 182177-71-5/BI OR 182177-72-6/BI OR
                 182177-73-7/BI OR 182177-74-8/BI OR 182177-75-9/BI OR 182177-76
                 -0/BI OR 182177-77-1/BI OR 182177-78-2/BI OR 182177-79-3/BI OR
                 182177-80-6/BI OR 182177-81-7/BI OR 182177-82-8/BI OR 182177-83
                 -9/BI OR 182177-84-0/BI OR 182177-85-1/BI OR 182177-86-2/BI OR
                 182177-87-3/BI OR 182177-88-4/BI OR 182177-89-5/BI OR 182177-90
                 -8/BI OR 182177-91-9/BI OR 182177-92-0/BI OR 182177-93-1/BI OR
                 182177-94-2/BI OR 182177-95-3/BI OR 182238-37-5/BI OR 182238-38
                 -6/BI OR 522671-88-1/BI OR 522671-89-2/BI OR 522672-79-3/BI OR
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                686373-48-8/BI) AND L24
                D QUE
                SAVE TEMP L86 MOH118SEQ/A

     FILE 'STNGUIDE' ENTERED AT 15:55:54 ON 23 FEB 2006

     FILE 'CAPLUS' ENTERED AT 15:57:47 ON 23 FEB 2006
                D QUE L14
L87           0 SEA ABB=ON  L14 NOT (L83 OR L85)

     FILE 'EMBASE' ENTERED AT 15:57:48 ON 23 FEB 2006
                D QUE L55
                D QUE L59
L88           4 SEA ABB=ON  (L55 OR L59) NOT L54

     FILE 'DRUGU' ENTERED AT 15:57:50 ON 23 FEB 2006
                D QUE L71
L89           0 SEA ABB=ON  L71 NOT L62

     FILE 'JICST-EPLUS, PASCAL, WPIX, IPA, BIOSIS, ESBIOBASE, BIOTECHDS,
     LIFESCI, CONFSCI, DISSABS, SCISEARCH' ENTERED AT 15:57:52 ON 23 FEB 2006
                D QUE L81
                D QUE L82
L90           6 SEA ABB=ON  (L81 OR L82) NOT L80

     FILE 'MEDLINE' ENTERED AT 15:57:59 ON 23 FEB 2006
                D QUE L42
                D QUE L44
L91           1 SEA ABB=ON  (L42 OR L44) NOT L37

     FILE 'STNGUIDE' ENTERED AT 15:58:07 ON 23 FEB 2006

     FILE 'MEDLINE, EMBASE, PASCAL, WPIX, BIOSIS, ESBIOBASE, SCISEARCH'
     ENTERED AT 15:58:31 ON 23 FEB 2006
L92           9 DUP REM L91 L88 L90 (2 DUPLICATES REMOVED)
                     ANSWER '1' FROM FILE MEDLINE
                     ANSWERS '2-5' FROM FILE EMBASE
                     ANSWER '6' FROM FILE PASCAL
                     ANSWERS '7-8' FROM FILE WPIX
                     ANSWER '9' FROM FILE BIOSIS
                D IALL 1-9

     FILE 'HOME' ENTERED AT 15:58:46 ON 23 FEB 2006
                D SAVED

=>
```

=> fil capl; d que l1; d que l5; s l1 or l5; fil medl; d que l37; fil embase; d que l54; fil drugu; d que l62
FILE 'CAPLUS' ENTERED AT 15:51:08 ON 23 FEB 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

FILE COVERS 1907 - 23 Feb 2006 VOL 144 ISS 9
FILE LAST UPDATED: 22 Feb 2006 (20060222/ED)

Effective October 17, 2005, revised CAS Information Use Policies apply.
They are available for your review at:

http://www.cas.org/infopolicy.html
'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L1 1 SEA FILE=CAPLUS ABB=ON US2003-660118/AP

inventor search

L3 2951 SEA FILE=CAPLUS ABB=ON WHITE C?/AU
L4 4538 SEA FILE=CAPLUS ABB=ON THIOREDOXIN#/OBI
L5 9 SEA FILE=CAPLUS ABB=ON L3 AND L4

L83 9 L1 OR L5

FILE 'MEDLINE' ENTERED AT 15:51:08 ON 23 FEB 2006

FILE LAST UPDATED: 22 FEB 2006 (20060222/UP). FILE COVERS 1950 TO DATE.

On December 11, 2005, the 2006 MeSH terms were loaded.

The MEDLINE reload for 2006 will soon be available. For details on the 2005 reload, enter HELP RLOAD at an arrow promt (=>).
See also:

http://www.nlm.nih.gov/mesh/
http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html

OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

Searched by Barb O'Bryen, STIC 2-2518

This file contains CAS Registry Numbers for easy and accurate

L35 2163 SEA FILE=MEDLINE ABB=ON THIOREDOXIN/CT
L36 2181 SEA FILE=MEDLINE ABB=ON WHITE C?/AU
L37 7 SEA FILE=MEDLINE ABB=ON L35 AND L36

FILE 'EMBASE' ENTERED AT 15:51:08 ON 23 FEB 2006

FILE COVERS 1974 TO 20 Feb 2006 (20060220/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate
substance identification.

L45 1505 SEA FILE=EMBASE ABB=ON WHITE C?/AU
L46 2331 SEA FILE=EMBASE ABB=ON THIOREDOXIN/CT
L54 8 SEA FILE=EMBASE ABB=ON L45 AND L46

FILE 'DRUGU' ENTERED AT 15:51:08 ON 23 FEB 2006

FILE LAST UPDATED: 23 FEB 2006 <20060223/UP>
>>> DERWENT DRUG FILE (SUBSCRIBER) <<<

>>> FILE COVERS 1983 TO DATE <<<
>>> THESAURUS AVAILABLE IN /CT <<<

L60 356 SEA FILE=DRUGU ABB=ON WHITE C?/AU
L61 72 SEA FILE=DRUGU ABB=ON THIOREDOXIN#/CT
L62 2 SEA FILE=DRUGU ABB=ON L60 AND L61

=> fil jic pascal wpix ipa biosis esbio biotechds lifesci confsci dissabs scisearch; d que l80
FILE 'JICST-EPLUS' ENTERED AT 15:51:25 ON 23 FEB 2006

FILE 'PASCAL' ENTERED AT 15:51:25 ON 23 FEB 2006

FILE 'WPIX' ENTERED AT 15:51:25 ON 23 FEB 2006

FILE 'IPA' ENTERED AT 15:51:25 ON 23 FEB 2006

FILE 'BIOSIS' ENTERED AT 15:51:25 ON 23 FEB 2006
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FILE 'SCISEARCH' ENTERED AT 15:51:25 ON 23 FEB 2006
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L72        11489 SEA WHITE C?/AU
L73        17233 SEA THIOREDOXIN#
L74        38537 SEA SPUTUM
L75        47183 SEA MUCUS
L76         3898 SEA MUCOLY?
L77        74427 SEA LIQUEF?
L78       567528 SEA VISCO?
L79        79051 SEA CYSTIC FIBROSIS
L80           10 SEA L72 AND L73 AND (L74 OR L75 OR L76 OR L77 OR L78 OR L79)
```

=> dup rem l37,l62,l83,l54,l80
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FILE 'DRUGU' ENTERED AT 15:51:39 ON 23 FEB 2006
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FILE 'ESBIOBASE' ENTERED AT 15:51:39 ON 23 FEB 2006

FILE 'BIOTECHDS' ENTERED AT 15:51:39 ON 23 FEB 2006

FILE 'SCISEARCH' ENTERED AT 15:51:39 ON 23 FEB 2006

PROCESSING COMPLETED FOR L37
PROCESSING COMPLETED FOR L62
PROCESSING COMPLETED FOR L83
PROCESSING COMPLETED FOR L54
PROCESSING COMPLETED FOR L80
L84 20 DUP REM L37 L62 L83 L54 L80 (16 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE MEDLINE
ANSWERS '8-9' FROM FILE DRUGU
ANSWERS '10-13' FROM FILE CAPLUS
ANSWERS '14-16' FROM FILE EMBASE
ANSWERS '17-18' FROM FILE PASCAL
ANSWERS '19-20' FROM FILE ESBIOBASE

=> d iall 1-9; d ibib ed abs hitind 10-13; d iall 14-20

L84 ANSWER 1 OF 20 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2005537349 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16214824
TITLE: Thioredoxin and dihydrolipoic acid inhibit elastase activity in cystic fibrosis sputum.
AUTHOR: Lee Rees L; Rancourt Raymond C; del Val Greg; Pack Kami; Pardee Churee; Accurso Frank J; **White Carl W**
CORPORATE SOURCE: Department of Pediatrics, National Jewish Medical and Research Center, Denver, CO 80206, USA.
CONTRACT NUMBER: HL-07670 (NHLBI)
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2005 Nov) 289 (5) L875-82.
Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 20051012
Last Updated on STN: 20051215
Entered Medline: 20051129
ABSTRACT:
Excessive neutrophil elastase activity within airways of cystic fibrosis (CF) patients results in progressive lung damage. Disruption of disulfide bonds on elastase by reducing agents may modify its enzymatic activity. Three naturally occurring dithiol reducing systems were examined for their effects on elastase activity: 1) Escherichia coli thioredoxin (Trx) system, 2) recombinant human thioredoxin (rhTrx) system, and 3) dihydrolipoic acid (DHLA). The Trx systems consisted of Trx, Trx reductase, and NADPH. As shown by spectrophotometric assay of elastase activity, the two Trx systems and DHLA inhibited purified human neutrophil elastase as well as the elastolytic activity present in the soluble phase (sol) of CF sputum. Removal of any of the three Trx system constituents prevented inhibition. Compared with the monothiols N-acetylcysteine and reduced glutathione, the dithiols displayed greater elastase inhibition. To streamline Trx as an investigational tool, a stable reduced form of rhTrx was synthesized and used as a single component. Reduced rhTrx inhibited purified elastase and CF sputum sol elastase without NADPH or

Trx reductase. Because Trx and DHLA have mucolytic effects, we investigated changes in elastase activity after mucolytic treatment. Unprocessed CF sputum was directly treated with reduced rhTrx, the Trx system, DHLA, or DNase. The Trx system and DHLA did not increase elastase activity, whereas reduced rhTrx treatment increased sol elastase activity by 60%. By contrast, the elastase activity after DNase treatment increased by 190%. The ability of Trx and DHLA to limit elastase activity combined with their mucolytic effects makes these compounds potential therapies for CF.

CONTROLLED TERM: Adult
Animals
Child
Comparative Study
*Cystic Fibrosis: DT, drug therapy
*Cystic Fibrosis: EN, enzymology
Enzyme Inhibitors: PD, pharmacology
Escherichia coli Proteins: PD, pharmacology
Humans
In Vitro
*Leukocyte Elastase: AI, antagonists & inhibitors
Rats
Recombinant Proteins: PD, pharmacology
Research Support, N.I.H., Extramural
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, Non-P.H.S.
Research Support, U.S. Gov't, P.H.S.
Sputum: EN, enzymology
*Thioctic Acid: AA, analogs & derivatives
Thioctic Acid: PD, pharmacology
***Thioredoxin: PD, pharmacology**

CAS REGISTRY NO.: 462-20-4 (dihydrolipoic acid); 52500-60-4 (Thioredoxin); 62-46-4 (Thioctic Acid)

CHEMICAL NAME: 0 (Enzyme Inhibitors); 0 (Escherichia coli Proteins); 0 (Recombinant Proteins); EC 3.4.21.37 (Leukocyte Elastase)

L84 ANSWER 2 OF 20 MEDLINE on STN DUPLICATE 6

ACCESSION NUMBER: 2004168104 MEDLINE

DOCUMENT NUMBER: PubMed ID: 14695120

TITLE: Thioredoxin liquefies and decreases the viscoelasticity of cystic fibrosis sputum.

AUTHOR: Rancourt Raymond C; Tai Shusheng; King Malcolm; Heltshe Sonya L; Penvari Churee; Accurso Frank J; **White Carl W**

CORPORATE SOURCE: National Jewish Medical and Research Center, 1400 Jackson St., Denver, CO 80206, USA.

CONTRACT NUMBER: HL-07670 (NHLBI)

SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2004 May) 286 (5) L931-8. Electronic Publication: 2003-12-24.
Journal code: 100901229. ISSN: 1040-0605.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200405

ENTRY DATE: Entered STN: 20040406
Last Updated on STN: 20040518
Entered Medline: 20040517

ABSTRACT:

The persistent and viscous nature of airway secretions in cystic fibrosis (CF) disease leads to airway obstruction, opportunistic infection, and deterioration

of lung function. Thioredoxin (Trx) is a protein disulfide reductase that catalyzes numerous thiol-dependent cellular reductive processes. To determine whether Trx can alter the rheological properties of mucus, sputum obtained from CF patients was treated with TRX and its reducing system (0.1 microM thioredoxin reductase + 2 mM NADPH), and liquid phase-gel phase ratio (percent liquid phase) was assessed by compaction assay. Exposure to low Trx concentrations (1 microM) caused significant increases in the percentage of liquid phase of sputum. Maximal increases in percent liquid phase occurred with 30 microM Trx. Additional measurements revealed that sputum liquefaction by the Trx reducing system is dependent on NADPH concentration. The relative potency of the Trx reducing system also was compared with other disulfide-reducing agents. In contrast with Trx, glutathione and N-acetylcysteine were ineffective in liquefying sputum when used at concentrations <1 mM. Sputum viscoelasticity, measured by magnetic microrheometry, also was diminished significantly following 20-min treatment with 3, 10, or 30 microM Trx. Similarly, this reduction in viscoelasticty also was dependent on NADPH concentration. Further investigation has indicated that Trx treatment increases the solubility of high-molecular-weight glycoproteins and causes redistribution of extracellular DNA into the liquid phase of sputum. Recognizing that mucins are the major gel-forming glycoproteins in mucus, we suggest that Trx alters sputum rheology by enzymatic reduction of glycoprotein polymers present in sputum.

CONTROLLED TERM: Check Tags: Female; In Vitro; Male
Adolescent
Adult
Cloning, Molecular
*Cystic Fibrosis: PP, physiopathology
Elasticity
Escherichia coli
Humans
Recombinant Proteins: PD, pharmacology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Rheology
Sputum: DE, drug effects
*Sputum: PH, physiology
***Thioredoxin: PD, pharmacology**
Viscosity

CAS REGISTRY NO.: 52500-60-4 (Thioredoxin)
CHEMICAL NAME: 0 (Recombinant Proteins)

L84 ANSWER 3 OF 20 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 1999170595 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10070119
TITLE: Induction of thioredoxin and thioredoxin reductase gene expression in lungs of newborn primates by oxygen.
AUTHOR: Das K C; Guo X L; **White C W**
CORPORATE SOURCE: Department of Pediatrics, National Jewish Medical and Research Center, Denver 80206; and University of Colorado Health Sciences Center, Denver, Colorado 80262, USA.. kumuda@uthct.edu
CONTRACT NUMBER: HL-52732 (NHLBI)
HL-53636 (NHLBI)
HL-56263 (NHLBI)
+
SOURCE: American journal of physiology, (1999 Mar) 276 (3 Pt 1) L530-9.
Journal code: 0370511. ISSN: 0002-9513.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199904
ENTRY DATE: Entered STN: 19990426
Last Updated on STN: 19990426
Entered Medline: 19990415

ABSTRACT:
Thioredoxin (TRX) is a potent protein disulfide oxidoreductase important in antioxidant defense and regulation of cell growth and signal transduction processes, among them the production of nitric oxide. We report that lung TRX and its reductase, TR, are specifically upregulated at birth by O2. Throughout the third trimester, mRNAs for TRX and TR were expressed constitutively at low levels in fetal baboon lungs. However, after premature birth (125 or 140 of 185 days gestation), lung TRX and TR mRNAs increased rapidly with the onset of O2 or air breathing. Lung TRX mRNA also increased in lungs of term newborns with air breathing. Premature animals (140 days) breathing 100% O2 develop chronic lung disease within 7-14 days. These animals had greater TRX and TR mRNAs after 1, 6, or 10 days of life than fetal control animals. In 140-day animals given lesser O2 concentrations (as needed) who do not develop chronic lung disease, lung TRX and TR mRNAs were also increased on days 1 and 6 but not significantly on day 10. In fetal distal lung explant culture, mRNAs for TRX and TR were elevated within 4 h in 95% O2 relative to 1% O2, and the response was similar at various gestations. In contrast, TRX protein did not increase in lung explants from premature animals (125 or 140 days) but did in those from near-term (175-day) fetal baboons after exposure to hyperoxia. However, lung TRX protein and activity, as well as TR activity, eventually did increase in vivo in response to hyperoxia (6 days). Increases in TRX and TR mRNAs in response to 95% O2 also were observed in adult baboon lung explants. When TRX redox status was determined, increased O2 tension shifted TRX to its oxidized form. Treatment of lung explants with actinomycin D inhibited TRX and TR mRNA increases in 95% O2, indicating transcriptional regulation by O2. The acute increase in gene expression for both TRX and TR in response to O2 suggests an important role for these proteins during the transition from relatively anaerobic fetal life to O2 breathing at birth.

CONTROLLED TERM:
Air
Animals
*Animals, Newborn: PH, physiology
Culture Techniques
Delivery, Obstetric
Fetus: ME, metabolism
*Gene Expression Regulation: DE, drug effects
Gene Expression Regulation: PH, physiology
Gestational Age
Humans
Infant, Newborn
*Lung: DE, drug effects
Lung: EM, embryology
Lung: ME, metabolism
Lung: PH, physiology
*Oxygen: PD, pharmacology
Papio
RNA, Messenger: ME, metabolism
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Respiration
Respiratory Distress Syndrome, Newborn: ME, metabolism
***Thioredoxin: GE, genetics**
*Thioredoxin Reductase (NADPH): GE, genetics

CAS REGISTRY NO.: 52500-60-4 (Thioredoxin); 7782-44-7 (Oxygen)
CHEMICAL NAME: 0 (RNA, Messenger); EC 1.6.4.5 (Thioredoxin Reductase

(NADPH))

L84 ANSWER 4 OF 20 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 1999351908 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10424622
TITLE: Hyperoxia induces thioredoxin and thioredoxin reductase gene expression in lungs of premature baboons with respiratory distress and bronchopulmonary dysplasia.
AUTHOR: Das K C; Guo X L; **White C W**
CORPORATE SOURCE: National Jewish Medical and Research Center and University of Colorado Health Sciences Center, Denver 80106, USA.
SOURCE: Chest, (1999 Jul) 116 (1 Suppl) 101S.
Journal code: 0231335. ISSN: 0012-3692.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199908
ENTRY DATE: Entered STN: 19990827
Last Updated on STN: 19990827
Entered Medline: 19990817
CONTROLLED TERM: Animals
*Bronchopulmonary Dysplasia: ME, metabolism
Humans
Infant, Newborn
*Oxygen: TO, toxicity
Papio
*Respiratory Distress Syndrome, Newborn: ME, metabolism
***Thioredoxin: GE, genetics**
*Thioredoxin Reductase (NADPH): GE, genetics
CAS REGISTRY NO.: 52500-60-4 (Thioredoxin); 7782-44-7 (Oxygen)
CHEMICAL NAME: EC 1.6.4.5 (Thioredoxin Reductase (NADPH))

L84 ANSWER 5 OF 20 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 1998278389 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9617827
TITLE: Detection of thioredoxin in human serum and biological samples using a sensitive sandwich ELISA with digoxigenin-labeled antibody.
AUTHOR: Das K C; **White C W**
CORPORATE SOURCE: Department of Pediatrics, National Jewish Medical and Research Center, Denver, CO 80206, USA.
CONTRACT NUMBER: HL46481 (NHLBI)
HL52732 (NHLBI)
HL56263 (NHLBI)
SOURCE: Journal of immunological methods, (1998 Feb 1) 211 (1-2) 9-20.
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199806
ENTRY DATE: Entered STN: 19980708
Last Updated on STN: 19980708
Entered Medline: 19980623
ABSTRACT:
Thioredoxin is a low molecular weight, redox active protein important in cellular proliferation, signal transduction and antioxidant function. Thioredoxin is secreted by normal as well as neoplastic cells and is

potentially involved in paracrine cell communication as suggested by its co-cytokine activity. Thus, the thioredoxin level in biological fluids, cells and tissue homogenates could be an important indicator of physiological or pathophysiological conditions. Hence, an accurate and sensitive measurement is of paramount importance in studies involving thioredoxin. We present here an ultrasensitive enzyme linked immuno-absorbent assay (ELISA) for human thioredoxin using digoxigenin-labelled goat polyclonal anti-human thioredoxin. The assay could detect a minimum level of 15 pg/ml thioredoxin in human serum, cell culture media, and in cell and tissue samples. The assay was optimized for concentration of both antibodies, blocking agent, plates, incubation time and reaction volumes. Excellent linearity and reproducibility were obtained. The assay was applied to different baboon tissues and human serum samples. The intrassay coefficient of variation (CV) was between 6.0 to 14 and the interassay CV was from 1.6 to 11.1. Excellent parallelism of standards with serum samples, tissue homogenates or cell lysates was obtained. More than 90% recovery of human thioredoxin was observed in 10% human serum. The assay is easy to use, rapid, reproducible, but above all it is a quantitative, specific and sensitive way to measure thioredoxin in a variety of biological specimens.

CONTROLLED TERM:
Animals
Antibodies
Asthma: BL, blood
Buffers
Calibration
Digoxigenin
Dose-Response Relationship, Drug
*Enzyme-Linked Immunosorbent Assay: MT, methods
Enzyme-Linked Immunosorbent Assay: ST, standards
Goats
Horseradish Peroxidase
Humans
Hydrogen-Ion Concentration
Indicators and Reagents
Papio: EM, embryology
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
Sensitivity and Specificity
***Thioredoxin: AN, analysis**
Thioredoxin: BL, blood
Time Factors

CAS REGISTRY NO.: 1672-46-4 (Digoxigenin); 52500-60-4 (Thioredoxin)
CHEMICAL NAME: 0 (Antibodies); 0 (Buffers); 0 (Indicators and Reagents); EC 1.11.1.- (Horseradish Peroxidase)

L84 ANSWER 6 OF 20 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1998072216 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9409558
TITLE: Elevation of manganese superoxide dismutase gene expression by thioredoxin.
AUTHOR: Das K C; Lewis-Molock Y; **White C W**
CORPORATE SOURCE: Department of Pediatrics, National Jewish Medical and Research Center, Denver, Colorado 80206, USA.
CONTRACT NUMBER: 1RO1 HL 52732 (NHLBI)
HL46481 (NHLBI)
SOURCE: American journal of respiratory cell and molecular biology, (1997 Dec) 17 (6) 713-26.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199801
ENTRY DATE: Entered STN: 19980122
Last Updated on STN: 19980122
Entered Medline: 19980107

ABSTRACT:
Manganese superoxide dismutase (MnSOD) is a mitochondrial enzyme that dismutates potentially toxic superoxide radical into hydrogen peroxide and dioxygen. This enzyme is critical for protection against cellular injury due to elevated partial pressures of oxygen. Thioredoxin (TRX) is a potent protein disulfide reductase found in most organisms that participates in many thiol-dependent cellular reductive processes and plays an important role in antioxidant defense, signal transduction, and regulation of cell growth and proliferation. Here we describe induction of manganese superoxide dismutase by thioredoxin. MnSOD mRNA and activity were increased dramatically by low concentrations of TRX (28 microM). Elevation of MnSOD mRNA by TRX was inhibited by actinomycin D, but not cycloheximide, occurring both in cell lines and primary human lung microvascular endothelial cells. mRNAs for other antioxidant enzymes including copper-zinc superoxide dismutase and catalase were not elevated, demonstrating specificity of induction of MnSOD by TRX. Thiol oxidation by diamide or alkylation by chlorodinitrobenzene inhibited MnSOD induction, further indicating a requirement for reduced TRX. Because both oxidized and reduced thioredoxin (28 microM) induced MnSOD mRNA, the intracellular redox status of externally added Escherichia coli oxidized TRX was determined. About 45% of internalized E. coli TRX was reduced, with 8% in fully reduced form and about 37% in partially reduced form. However, when TRX reductase and nicotinamide adenine dinucleotide (NADPH) were added to the extracellular medium with TRX, more than 80% of E. coli TRX was found to be in a fully reduced state in human adenocarcinoma (A549) cells. Although lower concentrations of oxidized TRX (7 microM) did not induce MnSOD mRNA, this concentration of TRX, when reduced by NADPH and TRX reductase, increased MnSOD mRNA six-fold. In additional studies, MCF-7 cells stably transfected with the human TRX gene had elevated expression of MnSOD mRNA relative to vector-transfected controls. Thus, both endogenously produced and exogenously added TRX elevate MnSOD gene expression. These findings suggest a novel mechanism involving reduced TRX in regulation of MnSOD.

CONTROLLED TERM:
Blotting, Western
Cells, Cultured
Cycloheximide: PD, pharmacology
Dactinomycin: PD, pharmacology
Diamide: PD, pharmacology
Dinitrochlorobenzene: PD, pharmacology
Dose-Response Relationship, Drug
Endothelium, Vascular: DE, drug effects
Endothelium, Vascular: EN, enzymology
Enzyme-Linked Immunosorbent Assay
Escherichia coli: ME, metabolism
*Gene Expression Regulation, Enzymologic: DE, drug effects
Humans
Kinetics
Lung: BS, blood supply
Oxidation-Reduction
RNA, Messenger: GE, genetics
Research Support, Non-U.S. Gov't
Research Support, U.S. Gov't, P.H.S.
*Superoxide Dismutase: GE, genetics
Superoxide Dismutase: ME, metabolism
***Thioredoxin: PD, pharmacology**
Tumor Cells, Cultured

CAS REGISTRY NO.: 10465-78-8 (Diamide); 50-76-0 (Dactinomycin); 52500-60-4 (Thioredoxin); 66-81-9 (Cycloheximide); 97-00-7

(Dinitrochlorobenzene)
CHEMICAL NAME: 0 (RNA, Messenger); EC 1.15.1.1 (Superoxide Dismutase)

L84 ANSWER 7 OF 20 MEDLINE on STN
ACCESSION NUMBER: 2002389710 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12122214
TITLE: Redox systems of the cell: possible links and implications.
COMMENT: Comment on: Proc Natl Acad Sci U S A. 2002 Jul 23;99(15):9745-9. PubMed ID: 12119401
AUTHOR: Das Kumuda C; **White Carl W**
CORPORATE SOURCE: Department of Molecular Biology, University of Texas at Tyler, 11937 U.S. Highway 271, Tyler, TX 75708, USA.
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2002 Jul 23) 99 (15) 9617-8. Electronic Publication: 2002-07-16.
Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Commentary
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200209
ENTRY DATE: Entered STN: 20020725
Last Updated on STN: 20030105
Entered Medline: 20020904
CONTROLLED TERM: *Glutathione: ME, metabolism
Glyceraldehyde-3-Phosphate Dehydrogenases: ME, metabolism
Humans
Oxidation-Reduction
***Thioredoxin: ME, metabolism**
CAS REGISTRY NO.: 52500-60-4 (Thioredoxin); 70-18-8 (Glutathione)
CHEMICAL NAME: EC 1.2.1.- (Glyceraldehyde-3-Phosphate Dehydrogenases)

L84 ANSWER 8 OF 20 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN DUPLICATE 3
ACCESSION NUMBER: 2005-23685 DRUGU B T
TITLE: Antioxidant defenses in the preterm lung: role for hypoxia-inducible factors in BPD
AUTHOR: Asikainen T M; **White C W**
CORPORATE SOURCE: Nat.Jewish-Med.+Res.Cent.
LOCATION: Denver, CO, USA
SOURCE: Toxicol.Appl.Pharmacol. (203, No. 2, 177-88, 2005) 3 Fig. 3 Tab. 136 Ref.
CODEN: TXAPA9 ISSN: 0041-008X
AVAIL. OF DOC.: Department of Pediatrics, National Jewish Medical and Research Center, Room D-301, 1400 Jackson Street, Denver, CO 80206, U.S.A. (e-mail: asikainent@njc.org).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

Antioxidant defenses in the preterm lung are reviewed. The role for hypoxia-inducible factors in bronchopulmonary dysplasia is discussed. Oxygen-induced lung injury and respiratory distress syndrome and pulmonary antioxidant defenses during development and in hyperoxia are described. The effects of various antioxidants and steroids (classical antioxidant enzymes, extracellular SOD, GSH and thioredoxin peroxidases and their associated reductases GSH and thioredoxin reductases, GSH and thioredoxin, heme oxygenases, and small molecular weight antioxidants (vitamins-C and -E), glucocorticoid, corticosteroids, selenium, inhaled nitric oxide) in preventing

bronchopulmonary dysplasia in preterm neonates are tabulated. This review suggests that single therapeutic factors are insufficient for successful treatment of a preterm baby at risk for developing bronchopulmonary dysplasia.

SECTION HEADING: B Biochemistry
T Therapeutics

CLASSIF. CODE: 22 Endogenous Compounds
33 Respiratory
67 Children and Elderly
69 Reviews

CONTROLLED TERM:
CASES *FT; IN-VIVO *FT; REVIEW *FT
[01] BRONCHOPULMONARY *TR; DYSPLASIA *TR; PNEUMOPATHY *TR; PREMATURE *FT; INFANT *FT; MAIN-TOPIC *FT; ANTIOXIDANT *FT; ANTIOXIDANTS *FT; PEDIATRICS *FT; TR *FT
[02] ORGOTEIN *TR; GLUTATHIONE *TR; **THIOREDOXIN** *TR; ASCORBATE *TR; TOCOPHEROL *TR; SELENIUM-SALT *TR; NITRIC-OXIDE *TR; TR *FT
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L84 ANSWER 9 OF 20 DRUGU COPYRIGHT 2006 THE THOMSON CORP on STN DUPLICATE 4
ACCESSION NUMBER: 2005-41456 DRUGU P B
TITLE: Thioredoxin and dihydrolipoic acid inhibit elastase activity in cystic fibrosis sputum.
AUTHOR: Lee R L; Rancourt R C; del Val G; Pack K; Pardee C; Accurso F J; **White C W**
CORPORATE SOURCE: Nat.Jewish-Med.Res.Cent.Denver; Jealot's-Hill.Int.Res.Cent.; Univ.Colorado
LOCATION: Denver, CO, USA; Bracknell, U.K.
SOURCE: AJP - Lung Cell.Mol.Physiol. (289, No. 5, L875-L882, 2005) 7 Fig. 41 Ref. ISSN: 1040-0605
AVAIL. OF DOC.: National Jewish Medical and Research Center, Dept. of Pediatrics, Rm. J318, 1400 Jackson St., Denver, CO 80206, U.S.A. (C.W.W.). (e-mail: whitec@njc.org).
LANGUAGE: English
DOCUMENT TYPE: Journal

ABSTRACT:

Dihydrolipoic acid (DHLA, dihydrothioctate) and thioredoxin (Trx) are known to decrease the viscoelasticity of cystic fibrosis (CF) mucus. The purpose of this in vitro study was to investigate the effect of DHLA and Trx on elastase activity after mucolytic treatment in CF adult and pediatric patients sputum. Both human (rhTrx) and E. coli recombinant Trx were investigated. Both Trx and DHLA inhibited human neutrophil elastase activity in CF sputum. The level of inhibition was significantly lower for pre-reduced rhTrx compared to rhTrx reduced in situ. A mucolytic effect was shown with pre-reduced rhTrx in whole unprocessed CF sputum but not with DHLA or Trx reduced in situ .The potential therapeutic use of Trx and DHLA, due to their combined elastase and mucolytic effect, in patients with CF is implied.

SECTION HEADING: P Pharmacology
B Biochemistry

CLASSIF. CODE: 14 Enzyme Inhibitors
33 Respiratory

CONTROLLED TERM:
CYSTIC-FIBROSIS *OC; PNEUMOPATHY *OC; CONGENITAL-DISEASE *OC; IN-VITRO *FT; CASES *FT; EC-3.4.21.11 *FT; INHIBITION *FT; MUCOLYTIC *FT; SPUTUM *FT; ELASTASE *FT
[01] THIOREDOXIN-HUMAN *PH; THIOREDHU *RN; RECOMBINANT *FT; PH *FT
[02] **THIOREDOXIN** *PH; THIOREDOX *RN; E.COLI *FT; RECOMBINANT *FT; GRAM-NEG. *FT; BACT. *FT; PH *FT
[03] DIHYDROTHIOCTATE *PH; DIHTHIOCT *RN; ANTIOXIDANTS *FT; PH *FT
CAS REGISTRY NO.: 462-20-4
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature

L84 ANSWER 10 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:1103433 CAPLUS
DOCUMENT NUMBER: 143:379832
TITLE: Use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous or cohesive mucus or sputum in patients with cystic fibrosis, chronic obstructive pulmonary disease or other disorders
INVENTOR(S): **White, Carl W.**; Del Val, Greg; Lee, Rees Livingston, II
PATENT ASSIGNEE(S): National Jewish Medical and Research Center, USA; Syngenta Limited; The United States Government
SOURCE: PCT Int. Appl., 123 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2005094269	A2	20051013	WO 2005-US10061		20050324
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW					
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
US 2005260140	A1	20051124	US 2005-90916		20050324
PRIORITY APPLN. INFO.:			US 2004-556516P	P	20040324
			US 2005-650865P	P	20050207
			US 2002-409960P	P	20020910
			US 2003-462082P	P	20030411
			US 2003-660118	A1	20030910

ED Entered STN: 14 Oct 2005
AB The present invention relates to the use of proteins or peptides comprising thioredoxin or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous or cohesive mucus or sputum in patients with cystic fibrosis, chronic obstructive pulmonary disease or

other disorders. The compns. contains a compound containing a dithiol active-site in reduced state such as thioredoxin and provides a reducing system for reducing said thioredoxin active site using NADPH and thioredoxin reductase. Respiratory diseases such as CF or COPD are amenable to treatment using compns. described above as well as various gastrointestinal or reproductive disorders.

IC ICM A61K

CC 1-9 (Pharmacology)
Section cross-reference(s): 63

IT **Thioredoxins**
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(active site, prokaryotic, yeast, plant, mammalian or human; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Drug delivery systems
(carriers; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Lung, disease
(chronic obstructive pulmonary disease; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Temperature effects, biological
(composition administered in absence of elevated; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Peptides, biological studies
Proteins
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(containing **thioredoxin** active site; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Thiols, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dithiols, active site, reduced form; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Physiological saline solutions
(hypertonic; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Drug delivery systems
(inhalants, composition administered via; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Drug delivery systems
(intratracheal, composition administered via; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Digestive tract
Reproductive system
Respiratory system

(mucus in; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Drug delivery systems
(nasal, composition administered via; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Drug delivery systems
(oral; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Embryophyta
Human
Mammalia
Plant
Prokaryota
Yeast
(**thioredoxin**; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT Cystic fibrosis
Mucus
Sputum
Viscosity
(use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT 9041-92-3, α1-Antitrypsin 37205-61-1, Proteinase inhibitor
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(composition administered in absence of; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT 53-57-6, Nadph 9074-14-0, **Thioredoxin** reductase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(for reducing **thioredoxin** active site of protein; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT 117525-19-6 866665-62-5
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**thioredoxin** active site sequence; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT 866669-22-9 866669-23-0 866669-24-1 866669-25-2 866669-26-3
866669-27-4 866669-28-5 866669-29-6 866669-30-9 866669-31-0
866669-32-1 866669-33-2
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(unclaimed protein sequence; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT 117525-18-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)

(unclaimed sequence; use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT 9004-06-2, Elastase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

IT 70-18-8, Glutathione, biological studies 462-20-4, Dihydrolipoic acid 1200-22-2, α-Lipoic acid 9003-98-9, DNase
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of proteins or peptides comprising **thioredoxin** or lipoic acid as mucolytic and anti-elastase agents for reducing excessively viscous mucous or sputum in CF or COPD patients)

L84 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 2004:252597 CAPLUS
DOCUMENT NUMBER: 140:281411
TITLE: Product and process using a protein or peptide having a **thioredoxin** active-site in a reduced state for liquefaction of mucus or sputum
INVENTOR(S): **White, Carl W.**
PATENT ASSIGNEE(S): National Jewish Medical and Research Center, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004024868	A2	20040325	WO 2003-US28526	20030910
WO 2004024868	A3	20050519		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2498581	AA	20040325	CA 2003-2498581	20030910
US 2004131606	A1	20040708	US 2003-660118	20030910 <--
EP 1551455	A2	20050713	EP 2003-752262	20030910
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				
US 2005260140	A1	20051124	US 2005-90916	20050324

PRIORITY APPLN. INFO.:

US 2002-409960P	P	20020910
US 2003-462082P	P	20030411
US 2003-660118	A1	20030910
WO 2003-US28526	W	20030910
US 2004-556516P	P	20040324
US 2005-650865P	P	20050207

ED Entered STN: 26 Mar 2004
AB The invention discloses compns. and methods for decreasing the viscosity and/or cohesiveness of and/or increasing the liquefaction of excessively

or abnormally viscous or cohesive mucus or sputum. The composition contains a protein or peptide containing a thioredoxin active-site in a reduced state and optionally further contains a reducing system.

IC ICM C12N

CC 1-12 (Pharmacology)
Section cross-reference(s): 63

ST mucus sputum liquefaction protein peptide reduced **thioredoxin** active site

IT Drug delivery systems
(bronchial; protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Drug delivery systems
(direct to lung; protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Drug delivery systems
(inhalants; protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Drug delivery systems
(intratracheal; protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Drug delivery systems
(nasal; protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Cystic fibrosis
Digestive tract
Drug delivery systems
Expectorants
Gastrointestinal agents
Human
Lung, disease
Mucus
Reproductive system
Respiratory system
Sputum
(protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT **Thioredoxins**
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Proteins
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Peptides, biological studies
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT DNA
Glycoproteins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sputum; protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT Embryophyta
Escherichia coli
Mammalia
Plant

Prokaryota
Yeast
(**thioredoxin** from; protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT 117525-19-6 675625-84-0 675625-85-1
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT 70-18-8, Glutathione, biological studies 616-91-1, N-Acetylcysteine 3483-12-3, Dithiothreitol
RL: PAC (Pharmacological activity); BIOL (Biological study)
(protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT 53-57-6, NADPH 9074-14-0, **Thioredoxin** reductase
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(protein or peptide with **thioredoxin** active-site in reduced state for liquefaction of mucus or sputum)

IT 675214-32-1 675214-33-2 675214-34-3 675214-35-4 675214-36-5 675214-37-6 675214-38-7 675214-39-8 675214-40-1 675214-41-2 675214-42-3 675214-43-4
RL: PRP (Properties)
(unclaimed protein sequence; product and process using a protein or peptide having a **thioredoxin** active-site in a reduced state for liquefaction of mucus or sputum)

IT 117525-18-5
RL: PRP (Properties)
(unclaimed sequence; product and process using a protein or peptide having a **thioredoxin** active-site in a reduced state for liquefaction of mucus or sputum)

L84 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 2002:576282 CAPLUS
DOCUMENT NUMBER: 137:306090
TITLE: Redox systems of the cell: Possible links and implications
AUTHOR(S): Das, Kumuda C.; **White, Carl W.**
CORPORATE SOURCE: Department of Molecular Biology, University of Texas at Tyler, Tyler, TX, 75708, USA
SOURCE: Proceedings of the National Academy of Sciences of the United States of America (2002), 99(15), 9617-9618
CODEN: PNASA6; ISSN: 0027-8424
PUBLISHER: National Academy of Sciences
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 04 Aug 2002
AB A review discussing a potential link between the two redox systems with glutathione and thioredoxin, and delineating the mechanism by which glutathionylation of thioredoxin can inactivate this multifunctional redox protein. The glutathione and thioredoxin systems are considered parallel redox systems, although their functions are distinct and divergent. Thioredoxin can mediate p53-dependent p21 activation, and thioredoxin translocates from the cytoplasm to the nucleus on stimulation by oxidative stress.
CC 6-0 (General Biochemistry)
ST review redox system glutathione **thioredoxin** oxidative stress
IT Redox potential
(biol.; role of glutathione and **thioredoxin** systems in

cellular redox status and oxidative stress)
IT Oxidative stress, biological
(role of glutathione and **thioredoxin** systems in cellular redox status and oxidative stress)
IT **Thioredoxins**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of glutathione and **thioredoxin** systems in cellular redox status and oxidative stress)
IT Substitution reaction
(thiolation, S-glutathionylation, biol.; role of glutathione and **thioredoxin** systems in cellular redox status and oxidative stress)
IT 70-18-8, Glutathione, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(role of glutathione and **thioredoxin** systems in cellular redox status and oxidative stress)
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1998:55547 CAPLUS
DOCUMENT NUMBER: 128:123821
TITLE: Use of **thioredoxin**-like molecules for induction of manganese-superoxide dismutase (MnSOD) to treat oxidative damage
INVENTOR(S): **White, Carl W.**; Das Kumuda, C.
PATENT ASSIGNEE(S): National Jewish Center for Immunology and Respiratory Medicine, USA
SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 9800160	A1	19980108	WO 1997-US11167		19970627
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG					
AU 9736434	A1	19980121	AU 1997-36434		19970627
US 5985261	A	19991116	US 1997-883804		19970627
PRIORITY APPLN. INFO.:			US 1996-20740P	P	19960628
			WO 1997-US11167	W	19970627

ED Entered STN: 30 Jan 1998
AB A method is provided to increase cellular MnSOD production in an animal to treat oxidative damage; the method involves administering a protein having a thioredoxin active-site in reduced state. A composition and a method to protect an animal from lung disease are provided.
IC ICM A61K038-19
ICS A61K038-16; A61K038-17
CC 1-12 (Pharmacology)
Section cross-reference(s): 63
ST oxidative damage SOD induction **thioredoxin** mol; lung disease SOD

induction **thioredoxin** mol; manganese superoxide dismutase induction oxidative damage

IT mRNA
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Mn-SOD; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Transcription factors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(NF-κB (nuclear factor κB); **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Lung, neoplasm
(adenocarcinoma; **thioredoxin** redox status in lung adenocarcinoma cells)

IT Respiratory distress syndrome
(adult, oxidative damage in; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Drug delivery systems
(bolus; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Drug delivery systems
(capsules; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Kidney
(cell; **thioredoxin** effect on Mn-SOD mRNA in different cell types)

IT Surfactants
(delivery vehicle; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Polymers, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(delivery vehicle; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Drug delivery systems
(diffusion devices; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Lung
(epithelium, cell; **thioredoxin** effect on Mn-SOD mRNA in different cell types)

IT Drug delivery systems
(inhalants; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Reperfusion
(injury, oxidative damage in; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Lung, disease
(interstitial, oxidative damage in; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Drug delivery systems
(intratracheal; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Drug delivery systems
(liposomes; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)

IT Drug delivery systems

(liposphereS; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Drug delivery systems
(microcapsules; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Drug delivery systems
(microparticles; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Blood vessel
Blood vessel
(microvessel, endothelium, cell; **thioredoxin** effect on Mn-SOD mRNA in different cell types)
IT Drug delivery systems
(nasal; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Respiratory distress syndrome
(newborn, oxidative damage in; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Drug delivery systems
(oral; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Drug delivery systems
(osmotic pumps; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Asthma
Atherosclerosis
Hyperoxia
Hypoxia, animal
Inflammation
Lung, disease
Neoplasm
(oxidative damage in; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Drug delivery systems
(parenterals; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Cell
(recombinant, delivery vehicle; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Drug delivery systems
(rectal; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Proteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**thioredoxin** active site-containing; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Fibroblast
(**thioredoxin** effect on Mn-SOD mRNA in different cell types)
IT Redox reaction
(**thioredoxin** redox status in lung adenocarcinoma cells)
IT Antioxidants
Drug delivery systems
Transcription, genetic
Translation, genetic
(**thioredoxin**-like mols. and compns. for induction of

manganese-superoxide dismutase to treat oxidative damage)
IT Escherichia coli
Mammal (Mammalia)
Prokaryote
Yeast
(**thioredoxin**; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Drug delivery systems
(transdermal; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT Actins
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(β-, mRNA; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT 9001-05-2, Catalase
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(mRNA; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT 9054-89-1, Superoxide dismutase
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(manganese-; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT 117525-18-5
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**thioredoxin** active site fragment sequence; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT 117525-19-6
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(**thioredoxin** active site sequence; **thioredoxin**-like mols. and compns. for induction of manganese-superoxide dismutase to treat oxidative damage)
IT 9074-14-0, **Thioredoxin** reductase
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**thioredoxin** redox status in lung adenocarcinoma cells)
REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L84 ANSWER 14 OF 20 EMBASE
ACCESSION NUMBER: 2004177414 EMBASE
TITLE: Thioredoxin liquefies and decreases the viscoelasticity of cystic fibrosis sputum.
AUTHOR: Rancourt R.C.; Tai S.; King M.; Heltshe S.L.; Penvari C.; Accurso F.J.; **White C.W.**
CORPORATE SOURCE: C.W. White, Natl. Jewish Med. and Res. Center, 1400 Jackson St., Denver, CO 80206, United States. whitec@njc.org
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2004) Vol. 286, No. 5 30-5, pp. L931-L938. .
Refs: 35

ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040520
Last Updated on STN: 20040520

ABSTRACT: The persistent and viscous nature of airway secretions in cystic fibrosis (CF) disease leads to airway obstruction, opportunistic infection, and deterioration of lung function. Thioredoxin (Trx) is a protein disulfide reductase that catalyzes numerous thiol-dependent cellular reductive processes. To determine whether Trx can alter the rheological properties of mucus, sputum obtained from CF patients was treated with TRX and its reducing system (0.1 μM thioredoxin reductase + 2 mM NADPH), and liquid phase-gel phase ratio (percent liquid phase) was assessed by compaction assay. Exposure to low Trx concentrations (1 μM) caused significant increases in the percentage of liquid phase of sputum. Maximal increases in percent liquid phase occurred with 30 μM Trx. Additional measurements revealed that sputum liquefaction by the Trx reducing system is dependent on NADPH concentration. The relative potency of the Trx reducing system also was compared with other disulfide-reducing agents. In contrast with Trx, glutathione and N-acetylcysteine were ineffective in liquefying sputum when used at concentrations <1 mM. Sputum viscoelasticity, measured by magnetic microrheometry, also was diminished significantly following 20-min treatment with 3, 10, or 30 μM Trx. Similarly, this reduction in viscoelasticty also was dependent on NADPH concentration. Further investigation has indicated that Trx treatment increases the solubility of high-molecular-weight glycoproteins and causes redistribution of extracellular DNA into the liquid phase of sputum. Recognizing that mucins are the major gel-forming glycoproteins in mucus, we suggest that Trx alters sputum rheology by enzymatic reduction of glycoprotein polymers present in sputum.

CONTROLLED TERM: Medical Descriptors:
*cystic fibrosis
*sputum
*liquefaction
*viscoelasticity
airway obstruction: CO, complication
opportunistic infection: CO, complication
reduction
gel
concentration response
flow measurement
mucus
Western blotting
DNA content
solubility
human
article
priority journal
Drug Descriptors:
***thioredoxin**
*glutathione
*acetylcysteine
*mucin: EC, endogenous compound
protein disulfide reductase (glutathione)
reduced nicotinamide adenine dinucleotide phosphate
CAS REGISTRY NO.: (thioredoxin) 52500-60-4; (glutathione) 70-18-8;

(acetylcysteine) 616-91-1; (protein disulfide reductase (glutathione)) 9082-53-5; (reduced nicotinamide adenine dinucleotide phosphate) 53-57-6
COMPANY NAME: American Diagnostica (United States); Sigma (United States); Fisher (United States)

L84 ANSWER 15 OF 20 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2002180321 EMBASE
TITLE: Complete pathway for protein disulfide bond formation encoded by poxviruses.
AUTHOR: Senkevich T.G.; **White C.L.**; Koonin E.V.; Moss B.
CORPORATE SOURCE: B. Moss, Laboratory of Viral Diseases, Natl. Inst. of Allerg./Infect. Dis., National Institutes of Health, Bethesda, MD 20892, United States. bmoss@nih.gov
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (14 May 2002) Vol. 99, No. 10, pp. 6667-6672. .
Refs: 27
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20020613
Last Updated on STN: 20020613

ABSTRACT: We show that three cytoplasmic thiol oxidoreductases encoded by vaccinia virus comprise a complete pathway for formation of disulfide bonds in intracellular virion membrane proteins. The pathway was defined by analyzing conditional lethal mutants and effects of cysteine to serine substitutions and by trapping disulfide-bonded heterodimer intermediates for each consecutive step. The upstream component, E10R, belongs to the ERV1/ALR family of FAD-containing sulfhydryl oxidases that use oxygen as the electron acceptor. The second component, A2.5L, is a small α-helical protein with a CxxxC motif that forms a stable disulfide-linked heterodimer with E10R and a transient disulfide-linked complex with the third component, G4L. The latter is a thioredoxin-like protein that directly oxidizes thiols of L1R, a structural component of the virion membrane with three stable disulfide bonds, and of the related protein F9L. These five proteins are conserved in all poxviruses, suggesting that the pathway is an ancestral mechanism for direct thiol-disulfide interchanges between proteins even in an unfavorable reducing environment.

CONTROLLED TERM: Medical Descriptors:
*virus assembly
protein assembly
disulfide bond
Poxvirus
Vaccinia virus
virion
lethal mutant
amino acid substitution
electron transport
alpha helix
protein structure
oxidation reduction reaction
protein expression
gene overexpression
covalent bond

nonhuman
article
priority journal
Drug Descriptors:
*thiol derivative
*oxidoreductase
*virus protein
*membrane protein
*flavine adenine nucleotide
*thiol oxidase
thioredoxin
epitope
CAS REGISTRY NO.: (thiol derivative) 13940-21-1; (oxidoreductase) 9035-73-8, 9035-82-9, 9037-80-3, 9055-15-6; (flavine adenine nucleotide) 146-14-5; (thiol oxidase) 9029-39-4; (thioredoxin) 52500-60-4

L84 ANSWER 16 OF 20 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1999122680 EMBASE
TITLE: Induction of thioredoxin and thioredoxin reductase gene expression in lungs of newborn primates by oxygen.
AUTHOR: Das K.C.; Guo X.-L.; **White C.W.**
CORPORATE SOURCE: K.C. Das, Dept. of Molecular Biology, Univ. of Texas Health Center, 11937 US Highway 271, Tyler, TX 75708-3154, United States. kumuda@uthct.edu
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (1999) Vol. 276, No. 3 20-3, pp. L530-L539. .
Refs: 50
ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
021 Developmental Biology and Teratology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 19990429
Last Updated on STN: 19990429

ABSTRACT: Thioredoxin (TRX) is a potent protein disulfide oxidoreductase important in antioxidant defense and regulation of cell growth and signal transduction processes, among them the production of nitric oxide. We report that lung TRX and its reductase, TR, are specifically upregulated at birth by O2. Throughout the third trimester, mRNAs for TRX and TR were expressed constitutively at low levels in fetal baboon lungs. However, after premature birth (125 or 140 of 185 days gestation), lung TRX and TR mRNAs increased rapidly with the onset of O2 or air breathing. Lung TRX mRNA also increased in lungs of term newborns with air breathing. Premature animals (140 days) breathing 100% O2 develop chronic lung disease within 7-14 days. These animals had greater TRX and TR mRNAs after 1, 6, or 10 days of life than fetal control animals. In 140-day animals given lesser O2 concentrations (as needed) who do not develop chronic lung disease, lung TRX and TR mRNAs were also increased on days 1 and 6 but not significantly on day 10. In fetal distal lung explant culture, mRNAs for TRX and TR were elevated within 4 h in 95% O2 relative to 1% O2, and the response was similar at various gestations. In contrast, TRX protein did not increase in lung explants from premature animals (125 or 140 days) but did in those from near-term (175- day) fetal baboons after exposure to hyperoxia. However, lung TRX protein and activity, as well as TR activity, eventually did increase in vivo in response to hyperoxia (6 days). Increases

in TRX and TR mRNAs in response to 95% O2 also were observed in adult baboon lung explants. When TRX redox status was determined, increased O2 tension shifted TRX to its oxidized form. Treatment of lung explants with actinomycin D inhibited TRX and TR mRNA increases in 95% O2, indicating transcriptional regulation by O2. The acute increase in gene expression for both TRX and TR in response to O2 suggests an important role for these proteins during the transition from relatively anaerobic fetal life to O2 breathing at birth.

CONTROLLED TERM: Medical Descriptors:
*gene expression
*oxygen breathing
*fetus lung maturation
primate
fetus lung
protein expression
antioxidant activity
cell growth
signal transduction
gene expression regulation
newborn period
prematurity
oxygen concentration
hyperoxia
lung dysplasia
respiratory distress
lung alveolus oxygen tension
nonhuman
animal experiment
controlled study
animal tissue
article
priority journal
Drug Descriptors:
***thioredoxin: EC, endogenous compound**
*thioredoxin reductase: EC, endogenous compound
*oxygen
nitric oxide: EC, endogenous compound

CAS REGISTRY NO.: (thioredoxin) 52500-60-4; (thioredoxin reductase) 9074-14-0; (oxygen) 7782-44-7; (nitric oxide) 10102-43-9

L84 ANSWER 17 OF 20 PASCAL COPYRIGHT 2006 INIST-CNRS. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2005-0473450 PASCAL

TITLE (IN ENGLISH): **Thioredoxin** and dihydrolipoic acid inhibit elastase activity in **cystic fibrosis sputum**

AUTHOR: LEE Rees L.; RANCOURT Raymond C.; DEL VAL Greg; PACK Kami; PARDEE Churee; ACCURSO Frank J.; **WHITE Carl W.**

CORPORATE SOURCE: Department of Pediatrics, National Jewish Medical and Research Center, Denver, Colorado, United States; Mike McMorris Cystic Fibrosis Center, University of Colorado Health Sciences Center, Denver, Colorado, United States; Jealott's Hill International Research Center, Bracknell, United Kingdom

SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2005), 33(5), L875-L882, 41 refs.

Searched by Barb O'Bryen, STIC 2-2518

ISSN: 1040-0605 CODEN: APLPE7
DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-22200, 354000135637220210
ABSTRACT: Excessive neutrophil elastase activity within airways of **cystic fibrosis** (CF) patients results in progressive lung damage. Disruption of disulfide bonds on elastase by reducing agents may modify its enzymatic activity. Three naturally occurring dithiol reducing systems were examined for their effects on elastase activity: I) Escherichia coli **thioredoxin** (Trx) system, 2) recombinant human **thioredoxin** (rhTrx) system, and 3) dihydrolipoic acid (DHLA). The Trx systems consisted of Trx. Trx reductase, and NADPH. As shown by spectrophotometric assay of elastase activity, the two Trx systems and DHLA inhibited purified human neutrophil elastase as well as the elastolytic activity present in the soluble phase (sol) of CF **sputum.** Removal of any of the three Trx system constituents prevented inhibition. Compared with the monothiols N-acetyl-cysteine and reduced glutathione, the dithiols displayed greater elastase inhibition. To streamline Trx as an investigational tool, a stable reduced form of rhTrx was synthesized and used as a single component. Reduced rhTrx inhibited purified elastase and CF **sputum** sol elastase without NADPH or Trx reductase. Because Trx and DHLA have **mucolytic** effects, we investigated changes in elastase activity after **mucolytic** treatment. Unprocessed CF **sputum** was directly treated with reduced rhTrx, the Trx system, DHLA, or DNase. The Trx system and DHLA did not increase elastase activity, whereas reduced rhTrx treatment increased sol elastase activity by 60%. By contrast, the elastase activity after DNase treatment increased by 190%. The ability of Trx and DHLA to limit elastase activity combined with their **mucolytic** effects makes these compounds potential therapies for CF.
CLASSIFICATION CODE: 002A20; Life sciences; Biological sciences; Vertebrates physiology, Respiratory system
002B22D05; Life sciences; Medical sciences; Metabolic diseases
CONTROLLED TERM: **Thioredoxin; Cystic fibrosis; Sputum;** Serine endopeptidases; Human; Mammalia; Respiratory system
BROADER TERM: Peptidases; Hydrolases; Enzyme; Vertebrata; Digestive diseases; Respiratory disease; Genetic disease; Metabolic diseases; Pancreatic disease

L84 ANSWER 18 OF 20 on STN PASCAL
ACCESSION NUMBER: 2004-0555882 PASCAL
COPYRIGHT NOTICE:
TITLE (IN ENGLISH): **Thioredoxin liquefies** and decreases the **viscoelasticity** of

cystic fibrosis sputum

AUTHOR: RANCOURT Raymond C.; SHUSHENG TAI; KING Malcolm; HELTSHE Sonya L.; PENVARI Churee; ACCURSO Frank J.; **WHITE Carl W.**

CORPORATE SOURCE: Department of Pediatrics, National Jewish Medical and Research Center, Denver 80206, United States; The Mike McMorris Cystic Fibrosis Research and Treatment Center, Department of Pediatrics, University of Colorado School of Medicine, Denver, Colorado 80218, United States; The Children's Hospital, Denver, Colorado 80218, United States; Pulmonary Research Group, University of Alberta, Edmonton, T6G 2S2, Canada

SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2004), 30(5), L931-L938, 35 refs.
ISSN: 1040-0605 CODEN: APLPE7

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-22200, 354000111659420050

ABSTRACT: The persistent and **viscous** nature of airway secretions in **cystic fibrosis** (CF) disease leads to airway obstruction, opportunistic infection, and deterioration of lung function. **Thioredoxin** (Trx) is a protein disulfide reductase that catalyzes numerous thiol-dependent cellular reductive processes. To determine whether Trx can alter the rheological properties of **mucus**, **sputum** obtained from CF patients was treated with TRX and its reducing system (0.1 μM **thioredoxin** reductase + 2 mM NADPH), and liquid phase-gel phase ratio (percent liquid phase) was assessed by compaction assay. Exposure to low Trx concentrations (1 μM) caused significant increases in the percentage of liquid phase of **sputum.** Maximal increases in percent liquid phase occurred with 30 μM Trx. Additional measurements revealed that **sputum liquefaction** by the Trx reducing system is dependent on NADPH concentration. The relative potency of the Trx reducing system also was compared with other disulfide-reducing agents. In contrast with Trx, glutathione and N-acetylcysteine were ineffective in **liquefying sputum** when used at concentrations <1 mM. **Sputum viscoelasticity**, measured by magnetic microrhe-ometry, also was diminished significantly following 20-min treatment with 3, 10, or 30 μM Trx. Similarly, this reduction in **viscoelasticty** also was dependent on NADPH concentration. Further investigation has indicated that Trx treatment increases the solubility of high-molecular-weight glycoproteins and causes redistribution of extracellular DNA into the liquid phase of **sputum.** Recognizing that mucins are the major gel-forming glycoproteins in **mucus**, we suggest that Trx alters **sputum** rheology by enzymatic reduction of glycoprotein polymers

present in **sputum.**

CLASSIFICATION CODE: 002A20; Life sciences; Biological sciences; Vertebrates physiology, Respiratory system
002B13C03; Life sciences; Medical sciences; Gastroenterology, Digestive system

CONTROLLED TERM: **Thioredoxin**; **Viscoelasticity**; **Cystic fibrosis**; **Sputum**; Mucin; **Mucus**; Glutathione; Acetylcysteine; Mammalia; Respiratory system

BROADER TERM: Vertebrata; Digestive diseases; Respiratory disease; Genetic disease; Metabolic diseases; Pancreatic disease; Thiol

L84 ANSWER 19 OF 20 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2005278476 ESBIOBASE

TITLE: **Thioredoxin** and dihydrolipoic acid inhibit elastase activity in **cystic fibrosis sputum**

AUTHOR: Lee R.L.; Rancourt R.C.; Val G.D.; Pack K.; Pardee C.; Accurso F.J.; **White C.W.**

CORPORATE SOURCE: C.W. White, National Jewish Medical and Research Center, Dept. of Pediatrics, 1400 Jackson St., Denver, CO 80206, United States.
E-mail: whitec@njc.org

SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2005), 289/5 33-5 (L875-L882), 41 reference(s)
CODEN: APLPE7 ISSN: 1040-0605

DOCUMENT TYPE: Journal; Article

COUNTRY: United States

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: Excessive neutrophil elastase activity within airways of **cystic fibrosis** (CF) patients results in progressive lung damage. Disruption of disulfide bonds on elastase by reducing agents may modify its enzymatic activity. Three naturally occurring dithiol reducing systems were examined for their effects on elastase activity: 1) Escherichia coli **thioredoxin** (Trx) system, 2) recombinant human **thioredoxin** (rhTrx) system, and 3) dihydrolipoic acid (DHLA). The Trx systems consisted of Trx, Trx reductase, and NADPH. As shown by spectrophotometric assay of elastase activity, the two Trx systems and DHLA inhibited purified human neutrophil elastase as well as the elastolytic activity present in the soluble phase (sol) of CF **sputum.** Removal of any of the three Trx system constituents prevented inhibition. Compared with the monothiols N-acetyl-cysteine and reduced glutathione, the dithiols displayed greater elastase inhibition. To streamline Trx as an investigational tool, a stable reduced form of rhTrx was synthesized and used as a single component. Reduced rhTrx inhibited purified elastase and CF **sputum** sol elastase without NADPH or Trx reductase. Because Trx and DHLA have **mucolytic** effects, we investigated changes in elastase activity after **mucolytic** treatment. Unprocessed CF

sputum was directly treated with reduced rhTrx, the Trx system, DHLA, or DNase. The Trx system and DHLA did not increase elastase activity, whereas reduced rhTrx treatment increased sol elastase activity by 60%. By contrast, the elastase activity after DNase treatment increased by 190%. The ability of Trx and DHLA to limit elastase activity combined with their **mucolytic** effects makes these compounds potential therapies for CF. Copyright .COPYRGT. 2005 the American Physiological Society.

CLASSIFICATION CODE: 99 General
SUPPLEMENTARY TERM: Thioctic acid; Serine protease; Lipoic acid; Human **thioredoxin**; **Mucolytic**

L84 ANSWER 20 OF 20 Elsevier BIOBASE COPYRIGHT 2006 Elsevier Science B.V. on STN

ACCESSION NUMBER: 2004108892 ESBIOBASE
TITLE: **Thioredoxin liquefies** and decreases the **viscoelasticity** of **cystic fibrosis sputum**
AUTHOR: Rancourt R.C.; Tai S.; King M.; Heltshe S.L.; Penvari C.; Accurso F.J.; **White C.W.**
CORPORATE SOURCE: C.W. White, Natl. Jewish Med. and Res. Center, 1400 Jackson St., Denver, CO 80206, United States. E-mail: whitec@njc.org
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2004), 286/5 30-5 (L931-L938), 35 reference(s)
CODEN: APLPE7 ISSN: 1040-0605
DOCUMENT TYPE: Journal; Article
COUNTRY: United States
LANGUAGE: English
SUMMARY LANGUAGE: English
ABSTRACT: The persistent and **viscous** nature of airway secretions in **cystic fibrosis** (CF) disease leads to airway obstruction, opportunistic infection, and deterioration of lung function. **Thioredoxin** (Trx) is a protein disulfide reductase that catalyzes numerous thiol-dependent cellular reductive processes. To determine whether Trx can alter the rheological properties of **mucus**, **sputum** obtained from CF patients was treated with TRX and its reducing system (0.1 μM **thioredoxin** reductase + 2 mM NADPH), and liquid phase-gel phase ratio (percent liquid phase) was assessed by compaction assay. Exposure to low Trx concentrations (1 μM) caused significant increases in the percentage of liquid phase of **sputum.** Maximal increases in percent liquid phase occurred with 30 μM Trx. Additional measurements revealed that **sputum liquefaction** by the Trx reducing system is dependent on NADPH concentration. The relative potency of the Trx reducing system also was compared with other disulfide-reducing agents. In contrast with Trx, glutathione and N-acetylcysteine were ineffective in **liquefying sputum** when used at concentrations <1 mM. **Sputum viscoelasticity**, measured by magnetic microrheometry, also was diminished significantly

following 20-min treatment with 3, 10, or 30 μM Trx. Similarly, this reduction in **viscoelasticty** also was dependent on NADPH concentration. Further investigation has indicated that Trx treatment increases the solubility of high-molecular-weight glycoproteins and causes redistribution of extracellular DNA into the liquid phase of **sputum.** Recognizing that mucins are the major gel-forming glycoproteins in **mucus** , we suggest that Trx alters **sputum** rheology by enzymatic reduction of glycoprotein polymers present in **sputum.**

CLASSIFICATION CODE: 99 General

SUPPLEMENTARY TERM: **Sputum viscoelasticity**; Mucin; **Mucus**; Glutathione; N-acetylcysteine; Deoxyribonucleic acid

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L7          4370 SEA FILE=CAPLUS ABB=ON  MUCUS/CT
L16          472 SEA FILE=CAPLUS ABB=ON  MUCOLY?/OBI
L17        29200 SEA FILE=CAPLUS ABB=ON  LIQUEF?/OBI
L18       161373 SEA FILE=CAPLUS ABB=ON  VISCO?/OBI
L19         1055 SEA FILE=CAPLUS ABB=ON  EXPECTORANT#/OBI
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L25       271004 SEA FILE=REGISTRY RAN=(,518362-12-4) ABB=ON  .C..C./SQSP
L26       269999 SEA FILE=REGISTRY ABB=ON  L24 NOT L25
L27        58456 SEA FILE=CAPLUS ABB=ON  L25 OR L26
L29           82 SEA FILE=CAPLUS ABB=ON  L27 AND (L6 OR L7)
L30            8 SEA FILE=CAPLUS ABB=ON  L29 AND (L16 OR L17 OR L18 OR L19)
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=> s l30 not l83
L85            6 L30 NOT L83
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previously printed w/ inventor search

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=> d ibib ed abs hitrn l85 1-6
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Note: It would have been too expensive to print all of the Registry records associated with these answers. If you find any hits that you particularly like, please return to me & I will print the associated Registry records.

L85 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:402755 CAPLUS
DOCUMENT NUMBER: 140:385998
TITLE: Sputum compaction assay for assessment of respiratory disease therapy
INVENTOR(S): Daugherty, Ann L.; Mrsny, Randy J.; Patapoff, Thomas W.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont. of U.S. Ser. No. 771,078.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003165810	A1	20030904	US 2002-162951	20020604
CA 2147469	AA	19940511	CA 1993-2147469	19931102
WO 9410567	A1	19940511	WO 1993-US10519	19931102
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9455464	A1	19940524	AU 1994-55464	19931102
EP 666985	A1	19950816	EP 1994-900497	19931102
EP 666985	B1	19970716		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 08502978	T2	19960402	JP 1993-511391	19931102
AT 155581	E	19970815	AT 1994-900497	19931102
ES 2106493	T3	19971101	ES 1994-900497	19931102
GR 3024987	T3	19980130	GR 1997-402630	19971009

AU 729265	B2	20010201	AU 1998-60676	19980407
US 2002034727	A1	20020321	US 2001-771078	20010125
US 2005164334	A1	20050728	US 2005-33358	20050110
PRIORITY APPLN. INFO.:			US 1992-971019	B1 19921102
			US 1993-132681	B1 19931006
			US 1994-355418	B1 19941213
			US 1995-539468	B1 19951005
			US 1997-840441	B1 19970401
			US 2001-771078	B1 20010125
			AU 1994-55464	A3 19931102
			WO 1993-US10519	W 19931102
			US 2002-162951	A1 20020604

ED Entered STN: 19 May 2004

AB A compaction assay measuring the viscoelasticity of sputum samples of patients subject to respiratory disease is provided. The compaction assay of the present invention is based upon the change in sputum compactability in a centrifugal field following in vitro DNase treatment of sputum, as measured by centrifugal pellet site which is related to the content of large-mol.-weight DNA. This assay is useful in determining the therapeutic efficacy of DNase, antibiotic and other respiratory disease treatments in improving lung function.

IT **686373-48-8**
RL: PRP (Properties)
(unclaimed protein sequence; sputum compaction assay for assessment of respiratory disease therapy)

L85 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:355745 CAPLUS
DOCUMENT NUMBER: 138:364735
TITLE: Characterization, recombinant production and sequence of an acidic mammalian chitinase, and its use in therapy or diagnosis of mucus-associated diseases or infectious diseases
INVENTOR(S): Aerts, Johannes Maria Franciscus Gerardus; Boot, Rolf Gabriel
PATENT ASSIGNEE(S): Neth.
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2003087414	A1	20030508	US 2001-4219	20011102
WO 2003038079	A2	20030508	WO 2002-NL694	20021101
WO 2003038079	A3	20030828		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1442119	A2	20040804	EP 2002-773037	20021101
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,				

IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK
US 2004253224 A1 20041216 US 2004-787845 20040226
PRIORITY APPLN. INFO.: US 2001-4219 A 20011102
WO 2002-NL694 W 20021101

ED Entered STN: 09 May 2003

AB The invention provides a mammalian mucinase capable of hydrolyzing mucin. Cloning, expression, sequences, physicochem. and enzymic properties of human and murine mucinase (acidic mammalian chitinase, AMCase) are described. The mucinase of the invention is among others suitable for counteracting diseases in which mucus is involved. These diseases comprise cystic fibrosis, COPD, asthma, bronchitis, tuberculosis, tumors with altered mucus expression, and mucus-containing pathogens. The invention also provides a pharmaceutical composition comprising an effective amount of the mucinase of the invention and a method of therapeutic or prophylactic treatment of an individual against a disease in which mucus is involved. Methods for obtaining the mucinase of the invention are also herewith provided, as well as nucleic acids encoding (part of) the mucinase. In one aspect the invention provides a diagnostic kit comprising a mucinase, a mucinase-specific antibody, a mucinase-derived peptide and/or nucleic acid encoding (part of) said mucinase.

IT **522671-88-1DP**, Chitinase (mouse acidic isoenzyme), subfragments are claimed **522671-89-2DP**, Chitinase (human acidic isoenzyme), subfragments are claimed
RL: ANT (Analyte); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); COS (Cosmetic use); DGN (Diagnostic use); FFD (Food or feed use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); PREP (Preparation); USES (Uses)
(amino acid sequence; characterization, recombinant production and sequence of acidic mammalian chitinase (mucinase), and its use in therapy or diagnosis of mucus-associated diseases or infectious diseases)

IT **522672-79-3**
RL: PRP (Properties)
(unclaimed protein sequence; characterization, recombinant production and sequence of an acidic mammalian chitinase, and its use in therapy or diagnosis of mucus-associated diseases or infectious diseases)

L85 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:122738 CAPLUS
DOCUMENT NUMBER: 136:194272
TITLE: Ribozymes and antisense oligonucleotides for the inhibition of gene expression by calcium-activated chloride channel-1 gene CLCA-1
INVENTOR(S): Thompson, James; McSwiggen, James; McKenzie, Timothy; Ayers, David; Szymkowski, David E.; Grupe, Andrew
PATENT ASSIGNEE(S): Ribozyme Pharmaceuticals, Incorporated, USA; Syntex (U.S.A.) LLC
SOURCE: PCT Int. Appl., 152 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002011674	A2	20020214	WO 2001-US24970	20010809
WO 2002011674	A3	20030925		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,

GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003064946 A1 20030403 US 2001-927046 20010809
PRIORITY APPLN. INFO.: US 2000-224383P P 20000809
ED Entered STN: 15 Feb 2002
AB Nucleic acid mols., including antisense and enzymic nucleic acid mols., such as hammerhead ribozymes, DNAzymes, and GeneBlocs, which modulate the expression of calcium-activated chloride channels (CLCA1, CLCA2, CLCA3, and CLCA4) are provided. A target discovery target validation approach was used for finding genes that are involved in chronic mucous hypersecretion. The reporter system consists of a plasmid construct, termed pMUC5AC-EGFP, bearing a gene coding for green fluorescent protein (GFP). The promoter region of the GFP gene is replaced by a portion of the mucin 5AC promoter sufficient to direct efficient transcription of the GFP gene; the plasmid also contains the neomycin drug resistance gene. The cell line selected as host for these studies, NCI-H292 (ATCC CRL-1848), is derived from a human lung mucoepidermoid carcinoma. A ribozyme library with two randomized regions comprising six-nucleotide binding "arms" is used to enrich cells for non-responders to mucin induction and a bioinformatics approach used to identify human CLCA1 as a regulator of MUC5AC expression. Antisense, hammerhead, DNAzyme, NCH, amberzyme, zinzyme, and G-Cleaver ribosome binding/cleavage sites in CLCA1 were identified. The nucleic acid mols. are individually analyzed by computer folding to assess whether the sequences fold into the appropriate secondary structure and to anneal to various sites in the RNA target. Those nucleic acid mols. with unfavorable intramol. interactions such as between the binding arms and the catalytic core are eliminated from consideration. Varying binding arm lengths can be chosen to optimize activity.
IT **143831-71-4**, Pulmozyme
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment in conjunction with; ribozymes and antisense oligonucleotides for the inhibition of gene expression by calcium-activated chloride channel-1 gene CLCA-1)

L85 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:616381 CAPLUS
DOCUMENT NUMBER: 125:266026
TITLE: Human DNase I variants with low affinity for actin for use in the treatment of respiratory disorders associated with **viscous** mucus
INVENTOR(S): Lazarus, Robert A.; Shak, Steven; Ulmer, Jana S.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9626279	A1	19960829	WO 1996-US2421	19960221

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,

ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN

WO 9626278	A1	19960829	WO 1995-US2366	19950224
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
ES 2188653	T3	20030701	ES 1995-912611	19950224
SK 284191	B6	20041005	SK 1997-1148	19950224
AU 9650263	A1	19960911	AU 1996-50263	19960221
AU 695863	B2	19980827		
BR 9607328	A	19971230	BR 1996-7328	19960221
EP 854927	A1	19980729	EP 1996-907094	19960221
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
PL 184951	B1	20030131	PL 1996-322002	19960221
RU 2215787	C2	20031110	RU 1997-115780	19960221
RO 118886	B1	20031230	RO 1997-1598	19960221
NO 9703877	A	19971024	NO 1997-3877	19970822
PRIORITY APPLN. INFO.:			WO 1995-US2366 A	19950224
			US 1995-540527 A	19951010
			EP 1995-912611 A	19950224
			WO 1996-US2421 W	19960221

ED Entered STN: 17 Oct 1996

AB Amino acid substitution variants of human DNase I that have reduced binding affinity for actin are described for use in the treatment of respiratory diseases where problems are associated with high-viscosity mucus, e.g. cystic fibrosis, chronic bronchitis. The variants are obtained by site-directed mutation of the cloned gene and therapeutically effective forms are manufactured by expression of the cloned gene. The invention also relates to pharmaceutical compns. and therapeutic uses of actin-resistant variants of human DNase I.

IT **182177-07-7**, Nuclease, deoxyribo-[13-alanine](human) **182177-08-8 182177-09-9**, Nuclease, deoxyribo-[13-arginine](human) **182177-10-2 182177-11-3**, Nuclease, deoxyribo-[13-tyrosine](human) **182177-12-4**, Nuclease, deoxyribo-[44-alanine](human) **182177-13-5 182177-14-6**, Nuclease, deoxyribo-[44-tyrosine](human) **182177-15-7 182177-16-8**, Nuclease, deoxyribo-[53-alanine](human) **182177-17-9**, Nuclease, deoxyribo-[53-lysine](human) **182177-18-0**, Nuclease, deoxyribo-[53-arginine](human) **182177-19-1**, Nuclease, deoxyribo-[53-tyrosine](human) **182177-20-4**, Nuclease, deoxyribo-[65-alanine](human) **182177-21-5**, Nuclease, deoxyribo-[65-arginine](human) **182177-22-6 182177-23-7**, Nuclease, deoxyribo-[67-alanine](human) **182177-24-8 182177-25-9**, Nuclease, deoxyribo-[67-lysine](human) **182177-26-0**, Nuclease, deoxyribo-[69-lysine](human) **182177-27-1**, Nuclease, deoxyribo-[69-arginine](human) **182177-28-2 182177-29-3 182177-30-6 182177-31-7 182177-32-8 182177-33-9**, Nuclease, deoxyribo-[44-cysteine](human) **182177-34-0 182177-35-1**, Nuclease, deoxyribo-[45-cysteine](human) **182177-36-2**, Nuclease, deoxyribo-[45-lysine](human) **182177-37-3**, Nuclease, deoxyribo-[45-

arginine](human) **182177-38-4**, Nuclease, deoxyribo-[48-cysteine](human) **182177-39-5**, Nuclease, deoxyribo-[48-lysine](human) **182177-40-8**, Nuclease, deoxyribo-[49-cysteine](human) **182177-41-9 182177-42-0**, Nuclease, deoxyribo-[49-lysine](human) **182177-43-1**, Nuclease, deoxyribo-[49-arginine](human) **182177-44-2**, Nuclease, deoxyribo-[49-tyrosine](human) **182177-45-3**, Nuclease, deoxyribo-[52-cysteine](human) **182177-46-4**, Nuclease, deoxyribo-[52-lysine](human) **182177-47-5 182177-48-6**, Nuclease, deoxyribo-[53-cysteine](human) **182177-49-7**, Nuclease, deoxyribo-[53-leucine](human) **182177-50-0 182177-51-1**, Nuclease, deoxyribo-[56-cysteine](human) **182177-52-2 182177-53-3**, Nuclease, deoxyribo-[56-lysine](human) **182177-54-4**, Nuclease, deoxyribo-[56-arginine](human) **182177-55-5 182177-56-6**, Nuclease, deoxyribo-[65-cysteine](human) **182177-57-7**, Nuclease, deoxyribo-[65-lysine](human) **182177-58-8 182177-59-9**, Nuclease, deoxyribo-[65-serine](human) **182177-60-2**, Nuclease, deoxyribo-[67-cysteine](human) **182177-61-3 182177-62-4 182177-63-5 182177-64-6**, Nuclease, deoxyribo-[67-proline](human) **182177-65-7**, Nuclease, deoxyribo-[67-arginine](human) **182177-66-8**, Nuclease, deoxyribo-[67-serine](human) **182177-67-9**, Nuclease, deoxyribo-[68-lysine](human) **182177-68-0 182177-69-1**, Nuclease, deoxyribo-[68-arginine](human) **182177-70-4**, Nuclease, deoxyribo-[69-alanine](human) **182177-71-5**, Nuclease, deoxyribo-[69-cysteine](human) **182177-72-6 182177-73-7 182177-74-8 182177-75-9**, Nuclease, deoxyribo-[114-glycine](human) **182177-76-0 182177-77-1**, Nuclease, deoxyribo-[114-lysine](human) **182177-78-2**, Nuclease, deoxyribo-[114-leucine](human) **182177-79-3 182177-80-6 182177-81-7 182177-82-8 182177-83-9 182177-84-0 182177-85-1 182177-86-2 182177-87-3 182177-88-4 182177-89-5 182177-90-8 182177-91-9 182177-92-0 182177-93-1 182177-94-2**, Nuclease, deoxyribo-[48-arginine](human) **182177-95-3 182238-37-5 182238-38-6**, Nuclease, deoxyribo-[65-proline](human)
RL: CAT (Catalyst use); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; human DNase I variants with low affinity for actin for use in treatment of respiratory disorders associated with **viscous** mucus)

IT **132053-08-8DP**, amino acid-substituted analogs
RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(human DNase I variants with low affinity for actin for use in treatment of respiratory disorders associated with **viscous** mucus)

L85 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1996:616378 CAPLUS
DOCUMENT NUMBER: 125:257176
TITLE: Human DNase I gene was mutated and enzyme was engineered for actin resistance and pharmaceutical use in reducing sputum **viscoelasticity** in lung disease treatment
INVENTOR(S): Lazarus, Robert A.; Shak, Steven; Ulmer, Jana S.
PATENT ASSIGNEE(S): Genentech, Inc., USA
SOURCE: PCT Int. Appl., 38 pp.

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9626278	A1	19960829	WO 1995-US2366	19950224
W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MN, MW, MX, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TT				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2210871	AA	19960829	CA 1995-2210871	19950224
AU 9519703	A1	19960911	AU 1995-19703	19950224
AU 720635	B2	20000608		
BR 9510323	A	19971111	BR 1995-10323	19950224
EP 811068	A1	19971210	EP 1995-912611	19950224
EP 811068	B1	20021218		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE				
HU 77422	A2	19980428	HU 1998-180	19950224
JP 11505408	T2	19990521	JP 1995-525640	19950224
PL 180773	B1	20010430	PL 1995-321890	19950224
CZ 288633	B6	20010815	CZ 1997-2677	19950224
AT 230027	E	20030115	AT 1995-912611	19950224
PT 811068	T	20030430	PT 1995-912611	19950224
ES 2188653	T3	20030701	ES 1995-912611	19950224
SK 283850	B6	20040302	SK 1997-1147	19950224
SK 284191	B6	20041005	SK 1997-1148	19950224
CA 2211413	AA	19960829	CA 1996-2211413	19960221
WO 9626279	A1	19960829	WO 1996-US2421	19960221
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK				
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AU 695863	B2	19980827		
BR 9607328	A	19971230	BR 1996-7328	19960221
PL 184951	B1	20030131	PL 1996-322002	19960221
RU 2215787	C2	20031110	RU 1997-115780	19960221
RO 118886	B1	20031230	RO 1997-1598	19960221
IL 117218	A1	20040601	IL 1996-117218	19960221
ZA 9601419	A	19970822	ZA 1996-1419	19960222
BG 64061	B1	20031128	BG 1997-101846	19970821
BG 64423	B1	20050131	BG 1997-101847	19970821
NO 9703876	A	19971024	NO 1997-3876	19970822
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NZ 334762	A	20001027	NZ 1999-334762	19990322
NZ 505985	A	20020201	NZ 2000-505985	20000726
US 2001041360	A1	20011115	US 2001-796774	20010228
US 6348343	B2	20020219		
PRIORITY APPLN. INFO.:			EP 1995-912611 A	19950224
			WO 1995-US2366	19950224
			US 1995-403873 B2	19950324

US 1995-540527	A	19951010
WO 1996-US2421	W	19960221
US 1997-929995	B1	19970915
NZ 1999-303837	A1	19990322
NZ 2000-282552	A1	20000726

ED Entered STN: 17 Oct 1996

AB The present invention relates to amino acid sequence variants of human DNase I that have reduced binding affinity for actin. The invention provides nucleic acid sequences encoding such actin-resistant variants, thereby enabling the production of these variants in quantities sufficient for clin. use. The invention also relates to pharmaceutical compns. and therapeutic uses of actin-resistant variants of human DNase I. DNase I variants are useful for reducing viscoelasticity of sputum in patients with cystic fibrosis or other pulmonary diseases or disorders.

IT **143831-71-4DP**, Nuclease, deoxyribo-(human clone 18-1 protein moiety), mutant derivs.
RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); PROC (Process); USES (Uses)
(human DNase I gene was mutated and enzyme was engineered for actin resistance and pharmaceutical use in reducing sputum **viscoelasticity** in lung disease treatment)

L85 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER:	1991:76410 CAPLUS
DOCUMENT NUMBER:	114:76410
TITLE:	Cloning and expression of cDNA for human pancreatic deoxyribonuclease I
INVENTOR(S):	Shak, Steven
PATENT ASSIGNEE(S):	Genentech, Inc., USA
SOURCE:	PCT Int. Appl., 50 pp. CODEN: PIXXD2
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9007572	A1	19900712	WO 1989-US5744	19891220
W: AU, JP				
RW: AT, BE, CH, DE, ES, FR, GB, IT, LU, NL, SE				
AU 9048265	A1	19900801	AU 1990-48265	19891220
AU 630658	B2	19921105		
EP 449968	A1	19911009	EP 1990-901443	19891220
EP 449968	B1	19990224		
R: AT, BE, CH, DE, ES, FR, GB, IT, LI, LU, NL, SE				
JP 04502406	T2	19920507	JP 1990-501900	19891220
JP 3162372	B2	20010425		
EP 853121	A2	19980715	EP 1998-105190	19891220
EP 853121	A3	19980805		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
AT 176924	E	19990315	AT 1990-901443	19891220
ES 2130120	T3	19990701	ES 1990-901443	19891220
JP 2001157580	A2	20010612	JP 2000-310722	19891220
CA 2006473	AA	19900623	CA 1989-2006473	19891221
CA 2006473	C	20020205		
US 2003044403	A1	20030306	US 2001-5675	20011107
US 2005009056	A1	20050113	US 2004-839046	20040504

PRIORITY APPLN. INFO.:	US 1988-289958	A	19881223

US 1989-448038	A	19891208
EP 1990-901443	A3	19891220
JP 1990-501900	A3	19891220
WO 1989-US5744	A	19891220
US 1992-914226	B3	19920713
US 1993-117584	B1	19930903
US 1995-528876	B1	19950915
US 1996-761578	B1	19961209
US 2000-669306	B1	20000925
US 2001-5675	B1	20011107

ED Entered STN: 09 Mar 1991

AB A cDNA encoding a human DNase I (DNase I) is cloned and expressed in Escherichia coli and mammalian cell culture. The enzyme is therapeutically useful for lowering the viscosity of sputum, for example in the treatment of cystic fibrosis without causing an immune response to the enzyme. The cDNA was cloned from a pancreatic cDNA library using oligonucleotide probes derived from the amino acid sequence of the bovine enzyme. Expression vectors for E. coli, HEK-293, and CHO cells were constructed using appropriate promoters. Transformants of E. coli with the plasmid pDNA11 (an expression-secretion vector) yielded up to 500 mg DNase I/L. Stable expression of the gene in CHO cells resulted in the manufacture of the enzyme at .apprx.0.05 pg/cell/day. The recombinant enzyme was shown to be capable of lowering the viscosity of sputum from cystic fibrosis patients (qual. determination).

IT **132053-07-7 132053-08-8**
RL: PRP (Properties)
(amino acid sequence of and expression in Escherichia coli and animal cell culture of gene for)

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FILE COVERS 1907 - 23 Feb 2006  VOL 144 ISS 9
FILE LAST UPDATED: 22 Feb 2006  (20060222/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE


L6          2350 SEA FILE=CAPLUS ABB=ON  SPUTUM/CT
L7          4370 SEA FILE=CAPLUS ABB=ON  MUCUS/CT
L11         3325 SEA FILE=CAPLUS ABB=ON  THIOREDOXINS/CT
L12            7 SEA FILE=CAPLUS ABB=ON  L11 AND (L6 OR L7)
L13       728128 SEA FILE=CAPLUS ABB=ON  9/SC,SX
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 FILE COVERS 1974 TO 20 Feb 2006 (20060220/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

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 substance identification.


L46         2331 SEA FILE=EMBASE ABB=ON  THIOREDOXIN/CT
L47         6283 SEA FILE=EMBASE ABB=ON  MUCUS+NT/CT
L48         3562 SEA FILE=EMBASE ABB=ON  SPUTUM/CT
L49          100 SEA FILE=EMBASE ABB=ON  SPUTUM VISCOSITY/CT
L50         3436 SEA FILE=EMBASE ABB=ON  VISCOELASTICITY/CT
L51         9749 SEA FILE=EMBASE ABB=ON  VISCOSITY/CT
L52          267 SEA FILE=EMBASE ABB=ON  MUCOLYSIS/CT
L53          183 SEA FILE=EMBASE ABB=ON  LIQUEFACTION/CT
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L56      20389 SEA FILE=EMBASE ABB=ON  CYSTIC FIBROSIS/CT
L59          1 SEA FILE=EMBASE ABB=ON  L46(L)DT/CT AND L56
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↑ subheading DT = drug therapy

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L88          4 (L55 OR L59) NOT L54
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previously printed

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FILE 'DRUGU' ENTERED AT 15:57:50 ON 23 FEB 2006
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FILE LAST UPDATED: 23 FEB 2006        <20060223/UP>
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>>>  FILE COVERS 1983 TO DATE  <<<
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L64       1059 SEA FILE=DRUGU ABB=ON  SPUTUM/CT
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L66        972 SEA FILE=DRUGU ABB=ON  MUCUS/CT
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L68         14 SEA FILE=DRUGU ABB=ON  LIQUEFACTION/CT OR LIQUEFYING/CT
L70      45091 SEA FILE=DRUGU ABB=ON  RESPIRATORY/CC
L71          1 SEA FILE=DRUGU ABB=ON  L61 AND (L63 OR L64 OR L65 OR L66 OR
               L67 OR L68) AND L70


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L89          0 L71 NOT L62
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previously printed

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scisearch; d que l81; d que l82

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FILE 'BIOTECHDS' ENTERED AT 15:57:52 ON 23 FEB 2006

FILE 'LIFESCI' ENTERED AT 15:57:52 ON 23 FEB 2006

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FILE 'DISSABS' ENTERED AT 15:57:52 ON 23 FEB 2006

FILE 'SCISEARCH' ENTERED AT 15:57:52 ON 23 FEB 2006


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L76         3898 SEA MUCOLY?
L81            8 SEA L73 AND L76



L73        17233 SEA THIOREDOXIN#
L74        38537 SEA SPUTUM
L75        47183 SEA MUCUS
L77        74427 SEA LIQUEF?
L78       567528 SEA VISCO?
L79        79051 SEA CYSTIC FIBROSIS
L82           14 SEA L73 AND (L74 OR L75) AND (L77 OR L78 OR L79)


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L90            6 (L81 OR L82) NOT L80

=> fil medl; d que l42; d que l44

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 FILE LAST UPDATED: 22 FEB 2006 (20060222/UP).  FILE COVERS 1950 TO DATE.

 On December 11, 2005, the 2006 MeSH terms were loaded.

 The MEDLINE reload for 2006 will soon be available.  For details
 on the 2005 reload, enter HELP RLOAD at an arrow promt (=>).
 See also:

    http://www.nlm.nih.gov/mesh/
    http://www.nlm.nih.gov/pubs/techbull/nd04/nd04_mesh.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_med_data_changes.html
    http://www.nlm.nih.gov/pubs/techbull/nd05/nd05_2006_MeSH.html
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OLDMEDLINE is covered back to 1950.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2006 vocabulary.

This file contains CAS Registry Numbers for easy and accurate

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L38        11646 SEA FILE=MEDLINE ABB=ON  SPUTUM/CT
L39        13832 SEA FILE=MEDLINE ABB=ON  VISCOSITY/CT
L40         8697 SEA FILE=MEDLINE ABB=ON  MUCUS+NT/CT
L42            3 SEA FILE=MEDLINE ABB=ON  L35 AND (L38 OR L39 OR L40)



L35         2163 SEA FILE=MEDLINE ABB=ON  THIOREDOXIN/CT
L43        19620 SEA FILE=MEDLINE ABB=ON  CYSTIC FIBROSIS/CT
L44            2 SEA FILE=MEDLINE ABB=ON  L43 AND L35


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previously printed

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PROCESSING COMPLETED FOR L91
PROCESSING COMPLETED FOR L88
PROCESSING COMPLETED FOR L90
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                 ANSWER '6' FROM FILE PASCAL
                 ANSWERS '7-8' FROM FILE WPIX
                 ANSWER '9' FROM FILE BIOSIS

=> d iall 1-9; fil hom
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L92 ANSWER 1 OF 9 MEDLINE on STN
ACCESSION NUMBER: 2002632750 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12391249
TITLE: A small molecule inhibitor of redox-regulated NF-kappa B and activator protein-1 transcription blocks allergic airway inflammation in a mouse asthma model.
AUTHOR: Henderson William R Jr; Chi Emil Y; Teo Jia-Ling; Nguyen Cu; Kahn Michael
CORPORATE SOURCE: Department of Medicine, University Washington, Seattle 98195, USA.. joangb@u.washington.edu
CONTRACT NUMBER: AI42989 (NIAID)
SOURCE: Journal of immunology (Baltimore, Md. : 1950), (2002 Nov 1) 169 (9) 5294-9.
Journal code: 2985117R. ISSN: 0022-1767.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021023
Last Updated on STN: 20021217
Entered Medline: 20021210

ABSTRACT:
An oxidant/antioxidant imbalance is seen in the lungs of patients with asthma. This oxidative stress in asthmatic airways may lead to activation of redox-sensitive transcription factors, NF-kappaB and AP-1. We examined the effect of the small molecule inhibitor of redox-regulated NF-kappaB and AP-1 transcription, MOL 294 on airway inflammation and airway hyperreactivity (AHR) in a mouse model of asthma. MOL 294 is a potent nonpeptide inhibitor of NF-kappaB and AP-1 based upon a beta-strand template that binds to and inhibits the cellular redox protein thioredoxin. BALB/c mice after i.p. OVA sensitization (day 0) were challenged with intranasal OVA on days 14, 25, 26, and 27. MOL 294, administered intranasal on days 25-27, blocked the airway inflammatory response to OVA assessed 24 h after the last OVA challenge on day 28. MOL 294 reduced eosinophil, IL-13, and eotaxin levels in bronchoalveolar lavage fluid and airway tissue eosinophilia and mucus hypersecretion. MOL 294 also decreased AHR in vivo to methacholine. These results support redox-regulated transcription as a therapeutic target in asthma and demonstrate that selective inhibitors can reduce allergic airway inflammation and AHR.

CONTROLLED TERM: Check Tags: Female
Administration, Intranasal
*Allergens: AD, administration & dosage
Animals
*Asthma: ME, metabolism
Asthma: PA, pathology
*Asthma: PC, prevention & control
Bronchial Hyperreactivity: PC, prevention & control
Bronchoalveolar Lavage Fluid: CY, cytology
Bronchoalveolar Lavage Fluid: IM, immunology
Cell Movement: DE, drug effects
Cell Movement: IM, immunology
Chemokines, CC: BI, biosynthesis
Disease Models, Animal
Eosinophils: DE, drug effects
Eosinophils: PA, pathology
Humans
Inflammation: ME, metabolism
Inflammation: PC, prevention & control
Interleukin-13: BI, biosynthesis
Lung: DE, drug effects

Lung: IM, immunology
*Lung: PA, pathology
Mice
Mice, Inbred BALB C
Mucus: DE, drug effects
Mucus: IM, immunology
Mucus: SE, secretion
*NF-kappa B: AI, antagonists & inhibitors
NF-kappa B: ME, metabolism
Ovalbumin: AD, administration & dosage
Ovalbumin: IM, immunology
Oxidation-Reduction: DE, drug effects
*Pyridazines: PD, pharmacology
Pyridazines: TU, therapeutic use
Research Support, U.S. Gov't, P.H.S.
Thioredoxin: AI, antagonists & inhibitors
*Transcription Factor AP-1: AI, antagonists & inhibitors
Transcription Factor AP-1: ME, metabolism
*Triazoles: PD, pharmacology
Triazoles: TU, therapeutic use
Tumor Cells, Cultured

CAS REGISTRY NO.: 52500-60-4 (Thioredoxin); 9006-59-1 (Ovalbumin)
CHEMICAL NAME: 0 (Allergens); 0 (Chemokines, CC); 0 (Interleukin-13); 0 (MOL 294); 0 (NF-kappa B); 0 (Pyridazines); 0 (Transcription Factor AP-1); 0 (Triazoles); 0 (eotaxin)

L92 ANSWER 2 OF 9 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2005547205 EMBASE
TITLE: Oxidants and COPD.
AUTHOR: MacNee W.
CORPORATE SOURCE: W. MacNee, ELEGI, Colt Research Laboratories, Medical School, Teviot Place, Edinburgh EH8 9AG, United Kingdom. w.macnee@ed.ac.uk
SOURCE: Current Drug Targets: Inflammation and Allergy, (2005) Vol. 4, No. 6, pp. 627-641. .
Refs: 162
ISSN: 1568-010X CODEN: CDTICU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20051222
Last Updated on STN: 20051222

ABSTRACT: Smoking is the main etiologic factor in chronic obstructive pulmonary disease (COPD). Cigarette smoke produces an enormous oxidant burden on the lungs, which is exacerbated by the release of oxidants from inflammatory cells. There is considerable evidence that an increased oxidative burden occurs in the lungs of patients with COPD, and this may be involved in many of the pathogenic processes, such as direct injury to lung cells, mucus hypersecretion, inactivation of antiproteases, and enhancing lung inflammation through activation of redox-sensitive transcription factors. COPD is also recognized to have multiple systemic consequences, such as weight loss and skeletal muscle dysfunction. Moreover, it is appreciated that oxidative stress

extends beyond the lung and may, through similar oxidative stress mechanisms as those in the lung, contribute to several of the systemic manifestations in COPD such as skeletal muscle dysfunction. Thus, there is a great need for an effective antioxidant therapy to modulate the oxidative stress in COPD, since this may be an important therapeutic target. .COPYRGT. 2005 Bentham Science Publishers Ltd.

CONTROLLED TERM: Medical Descriptors:
*chronic obstructive lung disease: DT, drug therapy
*chronic obstructive lung disease: ET, etiology
*chronic obstructive lung disease: PC, prevention
risk assessment
risk factor
cigarette smoking
air pollution
dietary intake
vitamin supplementation
disease exacerbation
inflammatory cell
pathogenesis
lung alveolus cell
cell damage
oxidation reduction reaction
weight reduction
body weight disorder: CO, complication
myopathy: CO, complication
oxidative stress
lung biopsy
pathophysiology
lymphocyte function
defense mechanism
lung alveolus epithelium
lung alveolus macrophage
in vitro study
signal transduction
forced expiratory volume
lung function test
breath analysis
lung lavage
lipid peroxidation
mucus secretion
bronchus mucus
gene expression regulation
gene silencing
virus infection
apoptosis
exercise
glutathione metabolism
muscle metabolism
muscle atrophy: CO, complication
protein expression
protein function
antioxidant activity
human
nonhuman
review
Drug Descriptors:
*oxidizing agent
proteinase inhibitor: EC, endogenous compound
transcription factor: EC, endogenous compound

reactive oxygen metabolite: EC, endogenous compound
reactive nitrogen species: EC, endogenous compound
cigarette smoke
nitric oxide: EC, endogenous compound
ozone
tumor necrosis factor alpha: EC, endogenous compound
lipopolysaccharide: EC, endogenous compound
xanthine dehydrogenase: EC, endogenous compound
superoxide: EC, endogenous compound
cytochrome P450: EC, endogenous compound
reduced nicotinamide adenine dinucleotide phosphate: EC, endogenous compound
nitric oxide synthase: EC, endogenous compound
aldehyde oxidase: EC, endogenous compound
flavoprotein: EC, endogenous compound
tryptophan 2,3 dioxygenase: EC, endogenous compound
iron
lipid peroxide
superoxide dismutase: EC, endogenous compound
catalase: EC, endogenous compound
glutathione: EC, endogenous compound
thioredoxin: EC, endogenous compound
ascorbic acid: DT, drug therapy
ascorbic acid: PD, pharmacology
beta carotene: DT, drug therapy
beta carotene: PD, pharmacology
flavonoid: DT, drug therapy
immunoglobulin enhancer binding protein: EC, endogenous compound
protein kinase: EC, endogenous compound
unindexed drug

CAS REGISTRY NO.: (proteinase inhibitor) 37205-61-1; (nitric oxide) 10102-43-9; (ozone) 10028-15-6; (xanthine dehydrogenase) 9054-84-6; (superoxide) 11062-77-4; (cytochrome P450) 9035-51-2; (reduced nicotinamide adenine dinucleotide phosphate) 53-57-6; (nitric oxide synthase) 125978-95-2; (aldehyde oxidase) 9029-07-6; (tryptophan 2,3 dioxygenase) 9014-51-1; (iron) 14093-02-8, 53858-86-9, 7439-89-6; (superoxide dismutase) 37294-21-6, 9016-01-7, 9054-89-1; (catalase) 9001-05-2; (glutathione) 70-18-8; (thioredoxin) 52500-60-4; (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (beta carotene) 7235-40-7; (protein kinase) 9026-43-1

L92 ANSWER 3 OF 9 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004119423 EMBASE

TITLE: Reduced Spectral Density Mapping of a Partially Folded Fragment of E. coli Thioredoxin.

AUTHOR: Daughdrill G.W.; Vise P.D.; Zhou H.; Yang X.; Yu W.-F.; Tasayco M.L.; Lowry D.F.

CORPORATE SOURCE: G.W. Daughdrill, Department of Microbiology, University of Idaho, P.O. Box 443052, Moscow, ID 83844-3052, United States. gdaugh@uidaho.edu

SOURCE: Journal of Biomolecular Structure and Dynamics, (2004) Vol. 21, No. 5, pp. 663-670. .
Refs: 18
ISSN: 0739-1102 CODEN: JBSDD6

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 004 Microbiology

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20040325
Last Updated on STN: 20040325
ABSTRACT: The backbone dynamics of a partially folded, N-terminal fragment of E. coli thioredoxin were investigated using nuclear magnetic resonance spectroscopy (NMR). Relaxation data were collected at three temperatures and analyzed using reduced spectral density mapping. As temperature was increased, the values for the viscosity normalized J(0) and for J(ω(H)) increased, while J(ω(N)) decreased. The global trend observed for the viscosity normalized J(0) was consistent with an increase in the hydrodynamic volume of the fragment and suggested the presence of correlated rotational motion in the absence of long range interactions. In addition, the residue specific variation observed for the viscosity normalized J(0) suggested contributions to J(ω) from a range of correlation times that are close to the global correlation time.

CONTROLLED TERM: Medical Descriptors:
*spectrometry
*protein folding
*Escherichia coli
molecular dynamics
amino terminal sequence
nuclear magnetic resonance spectroscopy
temperature
viscosity
hydrodynamics
rotation
protein interaction
correlation function
nonhuman
article
priority journal
Drug Descriptors:
***thioredoxin**
CAS REGISTRY NO.: (thioredoxin) 52500-60-4

L92 ANSWER 4 OF 9 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 2004512110 EMBASE
TITLE: The role of pyocyanin in Pseudomonas aeruginosa infection.
AUTHOR: Lau G.W.; Hassett D.J.; Ran H.; Kong F.
CORPORATE SOURCE: gee.lau@uc.edu
SOURCE: Trends in Molecular Medicine, (2004) Vol. 10, No. 12, pp. 599-606. .
Refs: 60
ISSN: 1471-4914 CODEN: TMMRCY
PUBLISHER IDENT.: S 1471-4914(04)00260-6
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
017 Public Health, Social Medicine and Epidemiology
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041217
Last Updated on STN: 20041217
ABSTRACT: Pyocyanin (PCN) is a blue redox-active secondary metabolite that is

produced by Pseudomonas aeruginosa. PCN is readily recovered in large quantities in sputum from patients with cystic fibrosis who are infected by P. aeruginosa. Despite in vitro studies demonstrating that PCN interferes with multiple cellular functions, its importance during clinical infection is uncertain. This is partially caused by the difficulty in defining the contribution of PCN among the numerous virulence factors produced by P. aeruginosa during infection. In addition, few cellular pathways that are affected by PCN are known. This review briefly highlights recent advances that might clarify the role of PCN in P. aeruginosa pathogenesis.

CONTROLLED TERM: Medical Descriptors:
*bacterial infection: DT, drug therapy
*bacterial infection: EP, epidemiology
*bacterial infection: ET, etiology
***cystic fibrosis: DT, drug therapy**
***cystic fibrosis: EP, epidemiology**
***cystic fibrosis: ET, etiology**
*molecular biology
*respiratory tract infection: DT, drug therapy
*respiratory tract infection: EP, epidemiology
*respiratory tract infection: ET, etiology
Pseudomonas aeruginosa
pathogenesis
correlation analysis
biosynthesis
operon
bacterial genome
bioaccumulation
bacterial virulence
protein synthesis
signal transduction
protein induction
molecular evolution
genetic code
transcription initiation
enzyme activation
genetic conservation
genetic variability
oxidation reduction reaction
gene targeting
Caenorhabditis elegans
Saccharomyces cerevisiae
enzyme inactivation
mitochondrial respiration
gene mutation
protein localization
gene expression
pathophysiology
protein depletion
oxidative stress
human
nonhuman
review
Drug Descriptors:
*pyocyanine
protein derivative: EC, endogenous compound
adenosine triphosphatase: EC, endogenous compound
antioxidant: DT, drug therapy
thioredoxin: DT, drug therapy
thioredoxin: PD, pharmacology

CAS REGISTRY NO.: (pyocyanine) 85-66-5; (adenosine triphosphatase) 37289-25-1, 9000-83-3; (thioredoxin) 52500-60-4

L92 ANSWER 5 OF 9 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2004465508 EMBASE
TITLE: Potential for antioxidant therapy of cystic fibrosis.
AUTHOR: Cantin A.M.
CORPORATE SOURCE: A.M. Cantin, Pulmonary Division, Dept. of Med. Faculty of Medicine, University of Sherbrooke, 3001, 12e Avenue Nord, Sherbrooke, Que. J1H 5N4, Canada.
andre.cantin@usherbrooke.ca
SOURCE: Current Opinion in Pulmonary Medicine, (2004) Vol. 10, No. 6, pp. 531-536. .
Refs: 42
ISSN: 1070-5287 CODEN: COPMFY
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20041129
Last Updated on STN: 20041129

ABSTRACT: Purpose of review: Changes in redox state clearly play a role in airway inflammation and mucus rheology. Furthermore CFTR (cystic fibrosis transmembrane conductance regulator), the defective protein in cystic fibrosis (CF), not only is regulated by redox state but also directly modulates the epithelial redox environment through transepithelial flux of glutathione. The purpose of this review is to explore the potential therapeutic interest of antioxidant molecules in CF. Recent findings: Several antioxidants have been shown to have mucolytic and anti-inflammatory properties. Some antioxidants such as zinc and vitamin C may also help increase epithelial chloride secretion through CFTR-dependent and independent pathways. Other antioxidants are showing promise in helping CFTR mobilization to plasma membranes. Summary: The many levels of potential application offered by antioxidants make this class of molecules one of the promising areas of therapeutic development for CF. Several redox-modulating agents have a high likelihood of providing useful approaches for the treatment of many aspects of CF airway disease.

CONTROLLED TERM: Medical Descriptors:
*cystic fibrosis: DT, drug therapy
oxidation reduction reaction
inflammation
mucus
lung infection
diet
chloride channel
genetic transcription
oxidative stress
gene expression
respiratory tract disease: SI, side effect
human
nonhuman
review
Drug Descriptors:
*antioxidant

*zinc: CB, drug combination
*zinc: PD, pharmacology
*ascorbic acid: PD, pharmacology
transmembrane conductance regulator: EC, endogenous compound
glutathione: DO, drug dose
glutathione: DT, drug therapy
glutathione: EC, endogenous compound
glutathione: PR, pharmaceutics
glutathione: IH, inhalational drug administration
chloride: EC, endogenous compound
reactive oxygen metabolite
nacystelyn: AE, adverse drug reaction
nacystelyn: DT, drug therapy
nacystelyn: PD, pharmacology
acetylcysteine: AE, adverse drug reaction
acetylcysteine: DT, drug therapy
acetylcysteine: PD, pharmacology
thioredoxin: EC, endogenous compound
reduced nicotinamide adenine dinucleotide phosphate
adenosine triphosphate
taurine
s nitrosoglutathione
curcumin: PD, pharmacology
selenocystine
glutathione derivative
alpha tocopherol succinate
alpha tocopherylquinone
thioctic acid
alpha tocopherol
immunoglobulin enhancer binding protein: EC, endogenous compound
protein kinase C: EC, endogenous compound
mucin: EC, endogenous compound
glutathione peroxidase: EC, endogenous compound
calnexin: EC, endogenous compound
calreticulin: EC, endogenous compound
epidermal growth factor receptor: EC, endogenous compound
toll like receptor 4: EC, endogenous compound
unindexed drug
unclassified drug

CAS REGISTRY NO.: (zinc) 7440-66-6; (ascorbic acid) 134-03-2, 15421-15-5, 50-81-7; (glutathione) 70-18-8; (chloride) 16887-00-6; (acetylcysteine) 616-91-1; (thioredoxin) 52500-60-4; (reduced nicotinamide adenine dinucleotide phosphate) 53-57-6; (adenosine triphosphate) 15237-44-2, 56-65-5, 987-65-5; (taurine) 107-35-7; (s nitrosoglutathione) 57564-91-7; (curcumin) 458-37-7; (selenocystine) 1464-43-3, 2897-21-4, 29621-88-3; (alpha tocopherol succinate) 17407-37-3, 4345-03-3; (alpha tocopherylquinone) 7559-04-8; (thioctic acid) 1077-29-8, 1200-22-2, 2319-84-8, 62-46-4; (alpha tocopherol) 1406-18-4, 1406-70-8, 52225-20-4, 58-95-7, 59-02-9; (protein kinase C) 141436-78-4; (glutathione peroxidase) 9013-66-5; (calnexin) 139873-08-8; (toll like receptor 4) 203811-83-0

L92 ANSWER 6 OF 9 PASCAL COPYRIGHT 2006 INIST-CNRS. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2004-0411858 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRGT. 2004 INIST-CNRS. All rights

TITLE (IN ENGLISH): Possible (enzymatic) routes and biological sites for metabolic reduction of BNP7787, a new protector against cisplatin-induced side-effects

AUTHOR: VERSCHRAAGEN Miranda; BOVEN Epie; TORUN Emine; HAUSHEER Frederick H.; BASF Aalt; VAN DER VIJGH Wim J. F.

CORPORATE SOURCE: Department of Medical Oncology, Vrije Universiteit medical center, De Boelelaan 1117, 1007MB Amsterdam, Netherlands; BioNumerik Pharmaceuticals, Inc., Ste. 400, 8122 Datapoint Drive, San Antonio, TX 78229, United States; Department of Pharmacology and Toxicology, University of Maastricht, P.O. Box 616, 6200MD Maastricht, Netherlands

SOURCE: Biochemical pharmacology, (2004), 68(3), 493-502, 22 refs.
ISSN: 0006-2952 CODEN: BCPCA6

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United States
LANGUAGE: English
AVAILABILITY: INIST-1418, 354000113766710100

ABSTRACT: Disodium 2,2'-dithio-bis-ethane sulfonate (BNP7787) is under investigation as a potential new chemoprotector against cisplatin-induced nephrotoxicity. The selective protection of BNP7787 appears to arise from the preferential uptake of the drug in the kidneys, where BNP7787 would undergo intracellular conversion into mesna (2-mercapto ethane sulfonate), which in turn can prevent cisplatin induced toxicities. In the present study, we have investigated whether the reduction of BNP7787 into the reactive compound mesna is restricted to the kidney or whether it can also occur in other organs, cells and physiological compartments, including the cytosolic fraction of the renal cortex, plasma, red blood cells (RBCs), liver and small intestine from rats and several tumors (OVCAR-3, MRI-H-207 and WARD). We also determined whether the endogenous thiols glutathione (GSH) and cysteine and the enzyme systems glutaredoxin and **thioredoxin**, which are all present in the kidney, can be involved in the BNP7787 reduction. UV detection and micro-HPLC with dual electrochemical detection were used to analyze the various incubation mixtures. Our observations are that, in contrast to plasma, a very large reductive conversion of BNP7787 to mesna was measured in RBC lysate. Intact RBCs, however, did not take up BNP7787. Although BNP7787 could be reduced in cytosol of liver and several tumors, this reduction will not be relevant in vivo, since these tissues do not take up large amounts of BNP7787. Kidney cortex cytosol was, similar to the small intestine cytosol, able to substantially reduce BNP7787 to mesna. The ability to reduce BNP7787 in the presence of the endogenous thiols GSH and cysteine, the glutaredoxin system as well as the **thioredoxin** system, could at least in part explain the high BNP7787 reductive activity of the kidney cortex cytosol. In conclusion, the high reduction of BNP7787 into mesna in the kidney as well

as our earlier observation that the distribution of BNP7787 and mesna was mainly restricted to rat kidney are strong arguments in favor of selective protection of the kidney by BNP7787.

CLASSIFICATION CODE: 002B02; Life sciences; Medical sciences; Pharmacology
CONTROLLED TERM: Cisplatin; Toxicity; Mesna; Kidney; **Thioredoxin**; Pharmacology; Antineoplastic agent; **Mucolytic**; Uroprotective agent
BROADER TERM: Alkylating agent; Urinary system

L92 ANSWER 7 OF 9 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-079352 [08] WPIX
DOC. NO. NON-CPI: N2006-068753
DOC. NO. CPI: C2006-028699
TITLE: Diagnosing Pseudomonas aeruginosa infection in a subject by detecting in a biological sample from the subject a protein of Pseudomonas aeruginosa, or its modified form, immunogenic fragment or epitope or antibody.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): PEDERSEN, S K; SLOANE, A J; WEINBERGER, R
PATENT ASSIGNEE(S): (PROT-N) PROTEOME SYSTEMS INTELLECTUAL PROPERTY P
COUNTRY COUNT: 111
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2006000056	A1	20060105	(200608)*	EN	103	G01N033-50

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW
W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2006000056	A1	WO 2005-AU942	20050628

PRIORITY APPLN. INFO: AU 2004-903521 20040628
INT. PATENT CLASSIF.:
MAIN: G01N033-50
SECONDARY: A61K039-104; A61K039-40; G01N033-53; G01N033-68
BASIC ABSTRACT:
WO2006000056 A UPAB: 20060201
NOVELTY - Diagnosing an infection caused by Pseudomonas aeruginosa in a subject comprising detecting in a biological sample from the subject a protein of Pseudomonas aeruginosa, a modified form of the protein or its immunogenic fragment or epitope or an antibody that binds to the protein, where the presence of the protein indicates the infection or exacerbation, is new.
DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:
(1) determining the response of a subject suffering from Pseudomonas aeruginosa infection to treatment with a therapeutic compound;
(2) diagnosing an acute pulmonary exacerbation in a subject suffering from **cystic fibrosis** or determining a **cystic**

fibrosis subject at risk of developing an acute pulmonary exacerbation which comprises diagnosing an infection caused by Pseudomonas aeruginosa in the subject, where diagnosis of the infection indicates that the subject is suffering from an acute pulmonary exacerbation or is at risk of developing an acute pulmonary exacerbation;

(3) determining the response of a subject having **cystic fibrosis** and suffering from an acute pulmonary exacerbation to treatment with a therapeutic compound for the exacerbation;

(4) treating a Pseudomonas aeruginosa infection in a subject or an acute pulmonary exacerbation in a subject suffering from **cystic fibrosis**;

(5) eliciting the production of an antibody against Pseudomonas aeruginosa which comprises administering the protein of Pseudomonas aeruginosa;

(6) a vaccine comprising the protein of Pseudomonas aeruginosa and a diluent; and

(7) a kit for detecting Pseudomonas aeruginosa infection in a biological sample.

ACTIVITY - Antibacterial.

No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The ferric iron-binding protein (HitA), **thioredoxin** dependent reductase (PAPS), **thioredoxin**, heat shock protein GroES, nucleotide dependent kinase (NDK) or DNA-binding protein HU is useful in the manufacture of a medicament for diagnosing Pseudomonas aeruginosa infection or an acute clinical exacerbation. The protein of Pseudomonas aeruginosa is useful in preparing a composition for treating or preventing Pseudomonas aeruginosa infection. (All claimed.)

Dwg.0/4

FILE SEGMENT: CPI EPI
FIELD AVAILABILITY: AB
MANUAL CODES: CPI: B04-B04B1; B04-B04D4; B04-B04D5; B04-B04G; B04-B04L; B04-F10A6; B04-G07; B04-G21; B04-G22; B04-N03C; B11-C07A; B12-K04A; B12-K04A4B; B14-A01A6; B14-S11B1; B14-S11D3; D05-H04; D05-H07; D05-H09; D05-H11
EPI: S03-E09F; S03-E14H

L92 ANSWER 8 OF 9 WPIX COPYRIGHT 2006 THE THOMSON CORP on STN
ACCESSION NUMBER: 2006-067567 [07] WPIX
DOC. NO. NON-CPI: N2006-058557
DOC. NO. CPI: C2006-024879
TITLE: Detection and/or dosing procedure for anti-transglutaminase antibodies in saliva sample uses immune reaction in pre-treated sample in conditions suitable for formation of immuno-complexes.
DERWENT CLASS: B04 D16 S03
INVENTOR(S): MASCART, F; OCMANT, A
PATENT ASSIGNEE(S): (ULBR) UNIV LIBRE BRUXELLES
COUNTRY COUNT: 111
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN IPC
WO 2005124344	A2	20051229	(200607)*	FR	29	G01N033-53

RW: AT BE BG BW CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IS IT KE LS LT LU MC MW MZ NA NL OA PL PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BW BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE EG ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG

KM KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NA NG NI
NO NZ OM PG PH PL PT RO RU SC SD SE SG SK SL SM SY TJ TM TN TR TT
TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2005124344	A2	WO 2005-EP6088	20050606

PRIORITY APPLN. INFO: WO 2004-EP6174 20040608
INT. PATENT CLASSIF.:
MAIN: G01N033-53
BASIC ABSTRACT:
WO2005124344 A UPAB: 20060130
NOVELTY - The procedure for detecting/dosing anti-transglutaminase antibodies in a saliva sample consists of pre-treating the sample with a **mucolytic** compound and then detecting the antibodies by an immune reaction with transglutaminase in conditions that are suitable for the formation of immuno-complexes with the antibodies.
DETAILED DESCRIPTION - The procedure for detecting/dosing anti-transglutaminase antibodies in a saliva sample consists of pre-treating the sample with a **mucolytic** compound and then detecting the antibodies by an immune reaction with transglutaminase in conditions that are suitable for the formation of immuno-complexes with the antibodies. The sampler is one with an activated indicator to show that quantity of the collected sample is adequate, and is selected from the group comprising: Omni-SAL (RTM), Salivette (RTM), Orapette (RTM) and OraSure (RTM). The mucalytic compound is selected from the group comprising: N-acetyl-cystein, nacystelyn, dithiothreitol, gelsolin, **thioredoxin** and EDTA.
USE - Detection of anti-transglutaminase antibodies in saliva for the detection of gluten-induced illnesses such as coeliac disease, or for monitoring a gluten-free regime.
ADVANTAGE - The procedure provides a simple, efficient and non-invasive solution for the diagnosis and monitoring of coeliac disease.
DESCRIPTION OF DRAWING(S) - The drawing shows a diagrammatic representation of the effects of diluting saliva with a preparation containing antigens. (Drawing contains non-English language text)
Dwg.1/11
FILE SEGMENT: CPI EPI
FIELD AVAILABILITY: AB; GI; DCN
MANUAL CODES: CPI: B04-G03; B10-B01B; B10-B02J; B10-E03; B11-C07A; B12-K04A; D05-H09
EPI: S03-E09F; S03-E14H2

L92 ANSWER 9 OF 9 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
DUPLICATE 1
ACCESSION NUMBER: 2005:492284 BIOSIS
DOCUMENT NUMBER: PREV200510285061
TITLE: An immunoproteomic approach for identification of clinical biomarkers for monitoring disease - Application to **cystic fibrosis.**
AUTHOR(S): Pedersen, Susanne K. [Reprint Author]; Sloane, Andrew J.; Prasad, Sindhu S.; Sebastian, Lucille T.; Lindner, Robyn A.; Hsu, Michael; Robinson, Michael; Bye, Peter T.; Weinberger, Ron P.; Harry, Jenny L.
CORPORATE SOURCE: Proteome Syst Ltd, 1-35-41 Waterloo Rd, N Ryde, NSW 2113, Australia

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SOURCE: Molecular & Cellular Proteomics, (AUG 2005) Vol. 4, No. 8, pp. 1052-1060.
ISSN: 1535-9476.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 16 Nov 2005
Last Updated on STN: 16 Nov 2005
ABSTRACT:Circulating antibodies can be used to probe protein arrays of body fluids, prepared by two-dimensional gel electrophoresis, for antigenic biomarker detection. However, detected proteins, particularly low abundance antigens, often remain unidentifiable due to proteome complexity and limiting sample amounts. Using a novel enrichment approach exploiting patient antibodies for isolation of antigenic biomarkers, we demonstrate how immunoproteomic strategies can accelerate biomarker discovery. Application of this approach as a means of identifying biomarkers was demonstrated for ***cystic*** **fibrosis** (CF) lung disease by isolation and identification of inflammatory-associated autoantigens, including myeloperoxidase and calgranulin B from **sputum** of subjects with CF. The approach was also exploited for isolation of proteins expressed by the Pseudomonas aeruginosa strain PA01. Capture of PA01 antigens using circulating antibodies from CF subjects implicated in vivo expression of Pseudomonas proteins. All CF subjects screened, but not controls, were immunoreactive against immunocaptured Pseudomonas proteins, representing stress (GroES and ferric iron-binding protein HitA), immunosuppressive (**thioredoxin**), and alginate synthetase pathway (nucleoside-diphosphate kinase) proteins, implicating their clinical relevance as biomarkers of infection.
CONCEPT CODE: Genetics - Human 03508
Clinical biochemistry - General methods and applications 10006
Enzymes - General and comparative studies: coenzymes 10802
Pathology - Diagnostic 12504
Metabolism - Metabolic disorders 13020
Digestive system - Pathology 14006
Respiratory system - Physiology and biochemistry 16004
Respiratory system - Pathology 16006
Physiology and biochemistry of bacteria 31000
Immunology - General and methods 34502
Immunology - Immunopathology, tissue immunology 34508
Medical and clinical microbiology - Bacteriology 36002
INDEX TERMS: Major Concepts
Infection; Methods and Techniques; Clinical Chemistry (Allied Medical Sciences); Clinical Immunology (Human Medicine, Medical Sciences)
INDEX TERMS: Parts, Structures, & Systems of Organisms
sputum: respiratory system
INDEX TERMS: Diseases
Pseudomonas aeruginosa infection: bacterial disease, diagnosis
INDEX TERMS: Diseases
cystic fibrosis: respiratory system disease, genetic disease, metabolic disease, digestive system disease, diagnosis
Cystic Fibrosis (MeSH)
INDEX TERMS: Chemicals & Biochemicals
antibodies; myeloperoxidase [EC 1.11.1.7]; calgranulin B; biomarkers: identification
INDEX TERMS: Methods & Equipment
two-dimensional gel electrophoresis: electrophoretic

techniques, laboratory techniques; immunoproteomics: laboratory techniques, immunologic techniques

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
human (common): host
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

ORGANISM: Classifier
Pseudomonadaceae 06508
Super Taxa
Gram-Negative Aerobic Rods and Cocci; Eubacteria; Bacteria; Microorganisms
Organism Name
Pseudomonas aeruginosa (species): pathogen, strain-PA01
Taxa Notes
Bacteria, Eubacteria, Microorganisms

REGISTRY NUMBER: 9003-99-0 (myeloperoxidase)
9003-99-0 (EC 1.11.1.7)

FILE 'HOME' ENTERED AT 15:58:46 ON 23 FEB 2006

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